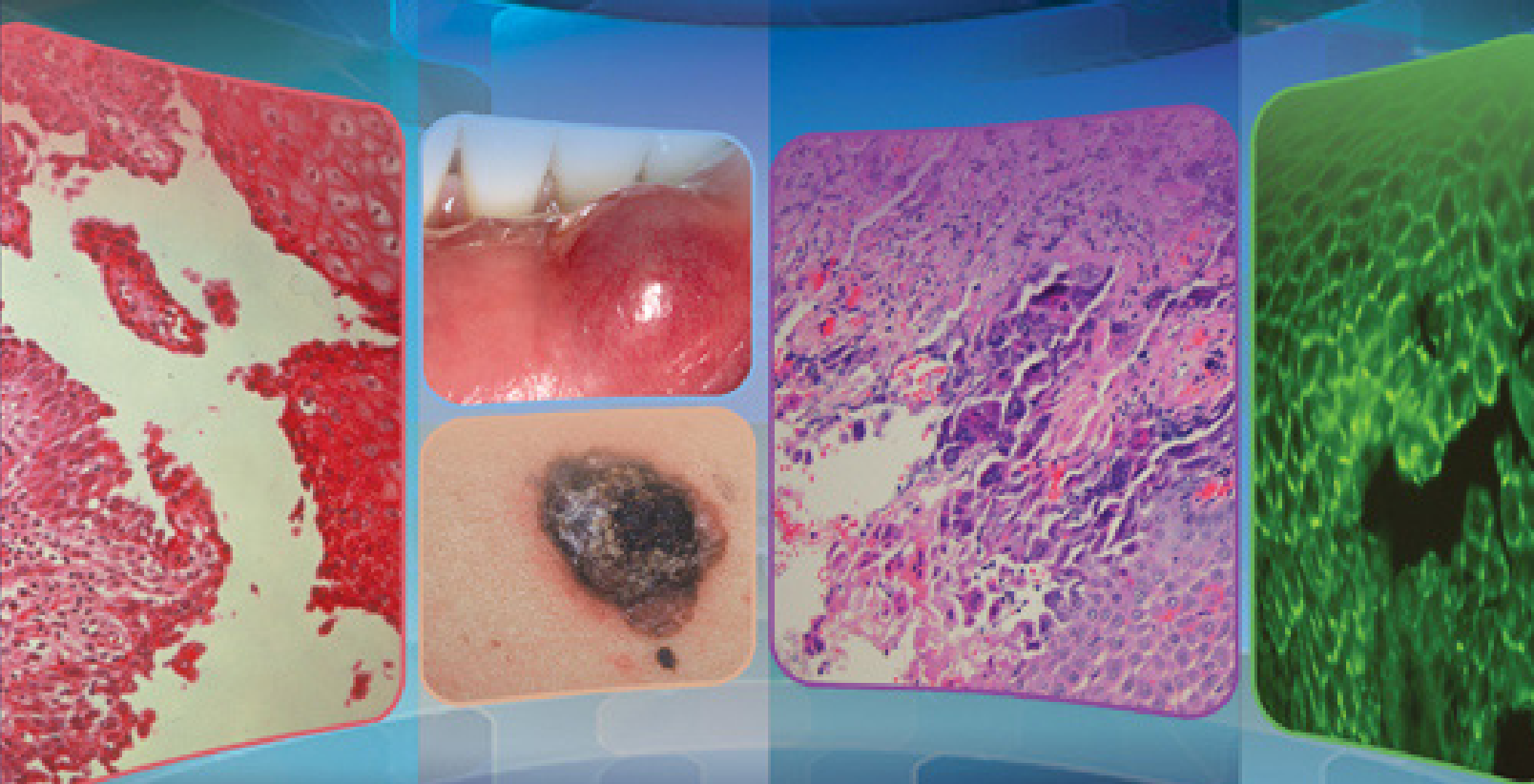
GENERAL AND ORAL PATHOLOGY FOR THE DENTAL HYGIENIST

SECOND EDITION



Leslie DeLong
Nancy W. Burkhart

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VISIT…

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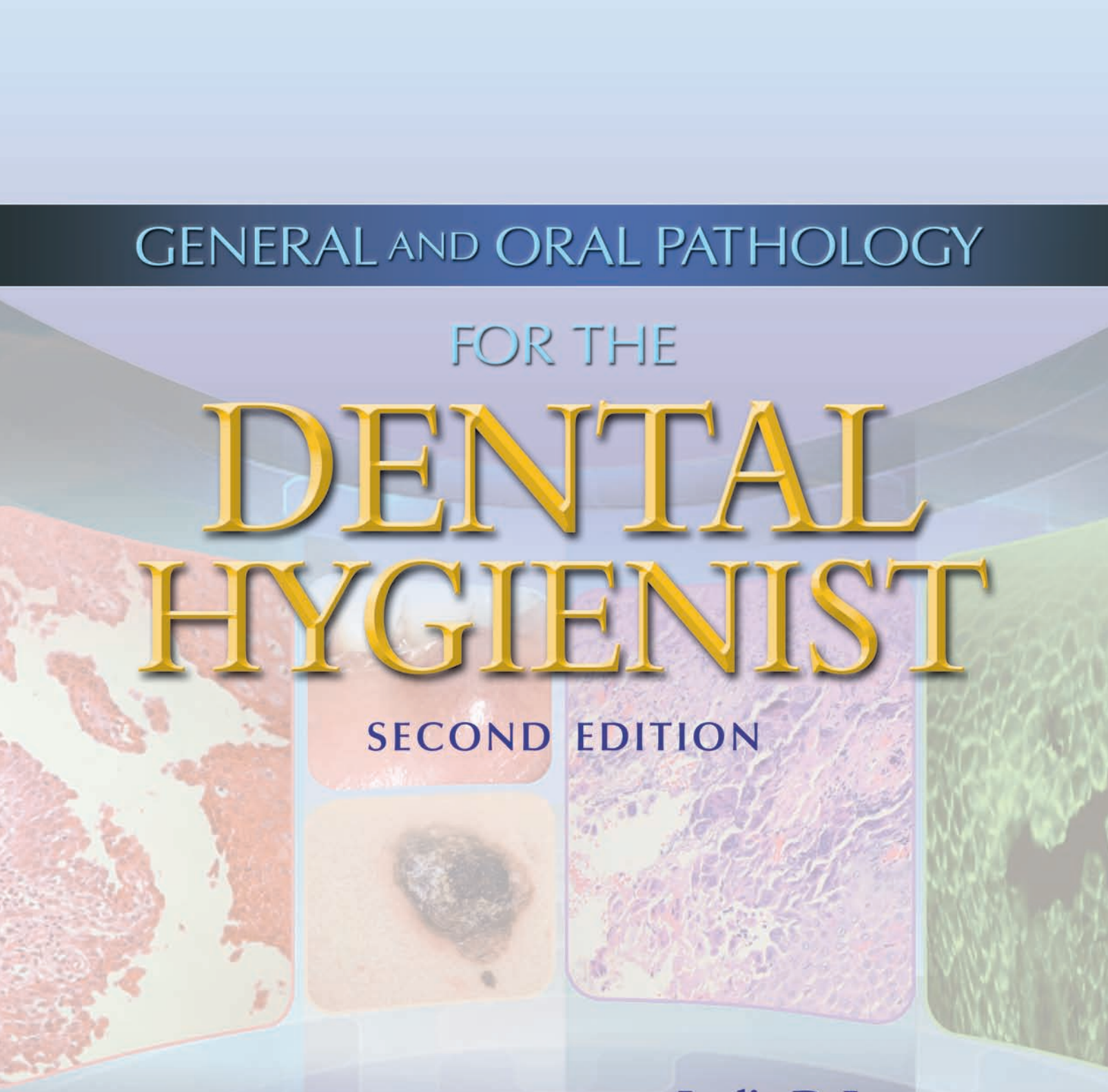

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Second Edition

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The second edition is dedicated to all of my past and present dental hygiene students. I am honored to have played a part in your education and have enjoyed watching you grow not only as adults but as professional dental hygienists. You have provided me with an education second to none and I thank you.

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PREFACE

General and Oral Pathology for the Dental Hygienist, 2nd Edition, is a comprehensive study of the general concepts of pathophysiology as they relate to systemic and oral conditions. The material is organized to provide students and practicing clinicians with the information they need in an easy to use format.

Chapter 1 is an overview of the head and neck and intraoral (cancer screening) examinations and the process of describing and documenting positive findings. Each element of a complete clinical and radiographic description is discussed including appropriate terminology, definitions, and images illustrating most of the terms. Documentation is explained in a clear and concise manner with ample opportunities for practice. Students will find this chapter an excellent supplement or reference for their preclinical and clinical courses, and practicing clinicians will find this chapter to be an excellent review for refining their skills.

Chapters 2 through 4 cover the basics of pathology, inflammation and repair, and the immune system, and are essential for understanding the remaining general and oral pathology chapters. Chapter 5, Neoplasia, continues coverage of basic pathology with a discussion of normal cell growth and regulation versus neoplastic cell growth, the process of carcinogenesis, cancer therapies, and description and discussion of various types of cancer. Chapter 6, Developmental, Genetic, and Congenital Disorders, completes coverage of the pathologic basis of disease with a brief discussion of these topics, including: morphogenesis, teratology, overview of genetic concepts, and a description of the various types of disorders using specific conditions as a basis for discussion.

Chapters 7 through 10 discuss disorders grouped into the following categories: Chapter 7, Endocrine Disorders; Chapter 8, Cardiovascular Disorders; Chapter 9, Blood Disorders; and Chapter 10, Respiratory, Gastrointestinal, Neurologic, and Skeletal Disorders. This quasi systems approach, whereby different systems are looked at from the viewpoint of a practicing dental hygienist reviewing a medical history, provides the student with a clear description of the pathogenesis of these conditions along with dental implications and treatment protocols. This information can not only be used in an Oral Pathology course but can also be used in clinical and preclinical courses and in courses dealing with treatment of medically compromised patients.

The second part of the book focuses on oral pathology. The different disorders are organized into categories or groups according to their distinctive clinical or radiographic features. Chapters 11 through 20 are separated into observable clinical or radiographic characteristics such as color (red or purple, white, pigmented), surface texture (rough or papillary), whether they are depressed (ulcers) or elevated (vesicles, soft or hard tissue enlargements) and finally whether they are radiolucent or radiopaque. This classification scheme becomes the first step in developing a differential diagnosis. In addition, it limits the number of conditions in each category, does not require the student or clinician to sift through numerous dissimilar lesions to get to the lesion most likely present, and gives the student or clinician something concrete to associate each lesion/condition with to increase retention of the information.

Chapter 21 focuses on tooth abnormalities and associated conditions and can be used to augment information in an oral anatomy and histology class as well as oral pathology classes. Chapter 23 is an excellent reference for identifying common cutaneous lesions seen during a head and neck examination. This information will be useful in determining a differential diagnosis and deciding on referral options for patients who present with skin lesions.

Chapter 22 provides in-depth coverage of oral lesions associated with HIV infection and AIDS including dental implications and current treatment options.

General and Oral Pathology for the Dental Hygienist includes many unique features created to enhance learning and provide opportunities for the practical application of information learned. These features include:

1. **Key Terms.** Key terms are listed at the beginning of the chapter and are bolded and defined within the text. In addition, each term is listed in a comprehensive glossary at the end of the book.
2. **Learner Objectives.** Learner objectives, located at the beginning of each chapter, help students focus on the key elements of material in the chapter.
3. **Chapter Outline.** Each chapter begins with an outline to make locating material within the chapter easier.
4. **Clinical Protocols.** References to numbered Clinical Protocols are made throughout the book and at the beginning of each chapter. Clinical protocols address the management of specific clinical or patient problems. They are excellent practice guidelines and references for the student and/or practicing clinician. The Clinical Protocols are found in the back of the book.
5. **Disease Lists.** The information related to specific oral and systemic diseases/conditions is organized in

a similar manner throughout the book. The template facilitates the learning process by allowing students to study the material in an organized fashion. The information is organized into the following categories:

- *Name*. The most common names and some of the less common or outdated names of the disorders are listed enabling the student to identify them when necessary.
- *Etiology*. The etiology of each disorder, if known, is identified in this section. In instances where the etiology is unknown, the prevailing theories of the etiology may be stated with information on the current focus of research.
- *Method of Transmission*. This section contains a concise description of how the disorder is transmitted; if appropriate, this includes the method of transmission of infectious organisms and inheritance patterns or genetic transmission.
- *Epidemiology*. Basic statistical information, such as incidence and prevalence, and information about the epidemiological aspects of each condition, such as age, sex, ethnicity, and geographical location, is essential for students to know in order to understand the disorders and to develop an appropriate differential diagnosis for a patient.
- *Pathogenesis*. Students need to know the why and the how of the disorders they are learning about in order to understand how the concepts of pathophysiology relate to them. As the students understand more, less memorization will be required. This section focuses on a brief description of how the disease/condition develops, detailing what happens on a cellular, tissue, or organ level and how the general health of the individual is affected.
- *Extraoral Characteristics*. Dental hygienists treat patients who present with a myriad of health problems. In order to properly assess patients and plan for appropriate dental hygiene care, the modern hygienist must be familiar with signs and symptoms of disease present in any area of the body. Clinically observable characteristics associated with the lower and upper body, and the head and neck area are described in this section.
- *Perioral and Intraoral Characteristics*. The perioral and intra oral manifestations of each disorder are comprehensively described in this section. In many instances, these manifestations are linked to systemic manifestations. As stated previously, lesions with similar perioral and/or oral characteristics are grouped together in the chapters dealing with oral lesions.
- *Distinguishing Characteristics*. This section identifies manifestations and sometimes microscopic or radiographic features that may only be associated with a specific disorder or group of similar disorders. This information is useful when developing a differential diagnosis.
- *Significant Microscopic Features*. Many of the conditions include a description of the histological appearance of the affected tissues and/or cells that can be crucial in helping students understand the pathological basis for the disorder. In addition, it is important for the student to know that microscopic examination is our only means of obtaining a definitive diagnosis for most lesions.
- *Dental Implications*. This section focuses on patient management issues associated with the specific diseases/conditions. Information related to patient assessment, treatment modifications, potential medical emergencies, homecare recommendations, and other topics, enables the student to be conscious of not only the specific disorder but also the impact the disorder may have on dental/dental hygiene treatment and on the individual's ability to perform self-care procedures.
- *Differential Diagnosis*. A differential diagnosis has been developed for many of the disorders. The differential diagnosis includes the names of disorders with similar manifestations and a reference to the chapter that discusses these disorders. Sometimes a brief explanation is included about why the condition is listed in the differential diagnosis. This is an excellent clinical reference for students and practicing clinicians.
- *Treatment and Prognosis*. The discussion of each disease/condition concludes with possible treatment methods and the prognosis associated with the disorder. The dental implications of specific therapeutic regimens may also be described in this section.

6. **Applications.** Applications, specific for each chapter, relate didactic knowledge to clinical practice. The applications may accomplish one or more of the following:
   - Describe how information just learned is encountered in everyday situations.
   - Expand on information for those who might be interested in more detail.
   - Suggest management techniques for patients who present with specific problems.
   - Relate systemic pathology to oral conditions and oral conditions to systemic pathology.
   - Discuss controversial or emerging issues and topics.
   - Suggest methods to educate patients about specific disorders.
7. **Chapter Summary.** Key points are summarized in a bulleted list at the conclusion of each chapter. The bullet points can be used to start discussions or help with self-study for examinations.

Chapter Review Section

1. **Case Studies.** The case studies associated with each chapter were developed to encompass all aspects of dental hygiene care and require the student to "put it all together." There are at least two case studies included in the text for each chapter, one introductory or basic case and one more advanced case. Both levels will challenge the student to use critical thinking to discover the answers; the more advanced cases may assume the student knows information not found in the chapter or may require some outside research to complete.
2. **Critical Thinking Activities.** These activities are included in each chapter and encourage the student to reach beyond memorizing the material to develop problem solving skills and to consider how the information will impact their practice of dental hygiene. These can be used to facilitate classroom and online discussions and could be used as a basis for a group project.
3. **Portfolio Possibilities.** More and more dental hygiene programs are requiring their students to produce portfolios showcasing self-evaluation and the achievement of specific program competencies. Therefore, each chapter includes suggestions for student-directed projects that would be useful in showing progress toward meeting competencies associated with patient care, health promotion, and disease prevention or professionalism. Many of the suggestions included in this section could be adapted for use as community service, service learning, or community health projects.
4. **Media Menu Resources.** Each chapter contains a representative sample of the internet resources found online at "thePoint" that can be accessed to enhance information included in the chapter. These include YouTube video clips illustrating various aspects of cellular pathology and other topics that may be of interest. As well as sites representing organizations such as The American Cancer Society and government sites such as The Centers for Disease Control and Prevention.
5. **Lesion/Condition Summary Tables.** These tables can be found at the end of every chapter starting with Chapter 4. They offer a brief concise summary of the essential information for each lesion/condition discussed in the chapter that can be used as a study aid for examinations and review for boards or to enhance clinical proficiency for practicing clinicians.

Student Resource Center

The Student Resource Center on thePoint includes review questions, additional case studies, and answers to the text case studies associated with each chapter.

- **Review questions** provide the student with the opportunity to check their understanding of the material in each chapter. Each question includes rationale for the correct answer as well as the rationale for why other choices are incorrect. Questions are formatted using the new Dental Hygiene National Board guidelines including multiple-multiple choice, ordering and matching questions, as well as the traditional multiple choice questions with five distractors.
- **Answers to each of the case studies in the text** are available for the student to check their ability to apply the information learned in the chapter and to prepare for case studies they may encounter in an examination.
- At least two **additional case studies** including answers are linked to each chapter to further strengthen the student's retention and application of knowledge learned.
- Extensive list of online resources that builds on the sample list seen in the chapter review section of the book. The student can utilize these resources to clarify concepts, acquire more in-depth information, obtain patient education materials and more.

See the inside front cover of this text for more details, including the passcode you will need to gain access to the Web site.

Instructor Resource Center

The Instructor Resource Center on thePoint has numerous aids for instructors:

- Detailed **PowerPoint presentations** are available for each chapter. The presentations may be modified to address the needs of the individual instructor.
- An **image bank** containing all of the images included in the text is available for use in classroom presentations or instructor-developed PowerPoint presentations.
- An **expanded list of the media resources** (including links to videos and animations) from each chapter's Media Menu facilitates using these resources for in-class presentations to explain concepts covered in chapters.
- At least **two additional case studies** (one basic and one more advanced) are included with each chapter and may be used for quizzes, tests, or classroom or online discussions.
- Instructors have access to **discussion points for the Critical Thinking Activities** listed at the end of each chapter. The critical thinking activities can be used to start a classroom or online discussion, or may be used as the basis for a group project. The discussion points give the instructor guidance for facilitating a discussion or the basis for evaluating a discussion or project.
- **Test bank questions** can be used to generate quizzes, tests, and final examinations. The questions are formatted according to Dental Hygiene National Board standards and include the same type of traditional multiple choice, multiple-multiple choice, ordering and matching questions that have been provided to the students.

The authors have endeavored to provide a comprehensive text that is user friendly and flexible enough to be adapted for use in dental hygiene education from the Associate degree to Master degree level. We feel confident you will be pleased with our efforts.

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Leslie DeLong
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CONTENTS

PART I GENERAL PATHOLOGY 1

CHAPTER 1 **Introduction to General and Oral Pathology** 2
Leslie DeLong

CHAPTER 2 **Basic Pathology** 29
Leslie DeLong

CHAPTER 3 **Inflammation and Repair** 45
Leslie DeLong

CHAPTER 4 **The Immune System and Immunity** 64
Leslie DeLong

CHAPTER 5 **Neoplasia** 85
Leslie DeLong

CHAPTER 6 **Developmental, Genetic, and Congenital Disorders** 117
Leslie DeLong

CHAPTER 7 **Endocrine Disorders** 159
Leslie DeLong

CHAPTER 8 **Cardiovascular Disorders** 193
Leslie DeLong

CHAPTER 9 **Blood Diseases** 226
Leslie DeLong

CHAPTER 10 **Respiratory, Gastrointestinal, Neurologic, and Skeletal Disorders** 262
Leslie DeLong

PART II ORAL PATHOLOGY 303

CHAPTER 11 **Lesions That Have a Vesicular Appearance** 304
Nancy W. Burkhart

CHAPTER 12 **Ulcers and Ulcer-Like Lesions** 331
Nancy W. Burkhart

CHAPTER 13 **Lesions in Shades of Red and Purple** 362
Nancy W. Burkhart

CHAPTER 14 **White Lesions** 385
John M. Wright

CHAPTER 15 **Pigmented Lesions** 409
Nancy W. Burkhart

CHAPTER 16 **Raised Lesions with a Rough or Papillary Surface** 433
Valerie Murrah

CHAPTER 17 **Soft Tissue Enlargements** 447
Valerie Murrah, Nancy W. Burkhart

CHAPTER 18 **Hard Tissue Enlargements** 484
Nancy W. Burkhart

CHAPTER 19 **Radiopaque Lesions** 504
Nancy W. Burkhart

CHAPTER 20 **Radiolucent Lesions** 517
Nancy W. Burkhart

CHAPTER 21 **Abnormalities of the Teeth** 549
Harvey P. Kessler

CHAPTER 22 **HIV and AIDS** 590
Jacqueline M. Plemons

CHAPTER 23 **Skin Lesions** 608
Nancy W. Burkhart

Appendix: Clinical Protocols 630

Glossary 664

Index 675

PART I

General Pathology

CHAPTER 1 **Introduction to General and Oral Pathology**
Leslie DeLong

CHAPTER 2 **Basic Pathology**
Leslie DeLong

CHAPTER 3 **Inflammation and Repair**
Leslie DeLong

CHAPTER 4 **The Immune System and Immunity**
Leslie DeLong

CHAPTER 5 **Neoplasia**
Leslie DeLong

CHAPTER 6 **Developmental,Genetic, and Congenital Disorders**
Leslie DeLong

CHAPTER 7 **Endocrine Disorders**
Leslie DeLong

CHAPTER 8 **Cardiovascular Disorders**
Leslie DeLong

CHAPTER 9 **Blood Diseases**
Leslie DeLong

CHAPTER 10 **Respiratory, Gastrointestinal, Neurologic, and Skeletal Disorders**
Leslie DeLong

CHAPTER 1

Introduction to General and Oral Pathology

KEY TERMS

Abrasion	Indurated
Amalgam tattoo	Lesion
Atypical	Localized
Benign	Lymphadenopathy
Biopsy	Macule
Bulla	Malignant
Circumscribed	Melanoma
Coalesced	Mixed
Convergent	Multilocular
Corrugated	Nodule
Crusted	Papillary
Definitive diagnosis	Papule
Differential diagnosis	Patch
Divergent	Pedunculated
Endogenous	Plaque
Endophytic	Pseudomembrane
Erosion	Pustule
Erythematic	Radiolucent
Exogenous	Radiopaque
Exophytic	Resorption
Exudate	Sessile
Purulent	Tumor
Fissured	Ulcer
Fluctuant	Unilocular
Generalized	Vesicle
Homeostasis	

LEARNING OUTCOMES

1. Define and use the key terms in this chapter.
2. Discuss the concept of "wellness."
3. Describe the changing roles of the patient and the clinician.
4. State the objectives of the clinical evaluation.
5. Describe the elements of an extraoral and intraoral examination or oral cancer screening.
6. List observations that might suggest that a lesion is benign or malignant.
7. Note the elements of a complete clinical description.
8. List the elements that should be included in a description of radiographic findings.
9. Write a complete clinical description of a sample case study.
10. Describe the steps involved in reaching a differential diagnosis.
11. Describe possible ways of determining a definitive diagnosis.

CHAPTER OUTLINE

Health and Wellness
Disease
The Role of the Dental Hygienist
Objectives of the Clinical Evaluation
  Performing an Extraoral Examination
  Performing an Intraoral Examination
  Describing and Recording Clinical Findings
    History
    Location
    Distribution and definition
    Size and shape
    Color
    Consistency
    Surface texture
  Describing Radiographic Findings
    History
    Location and size
    Distribution
    Radiographic features
Determining a Diagnosis
  Differential Diagnosis
  Definitive Diagnosis

RELATED CLINICAL PROTOCOL

#15 Office Protocol for Identifying Suspected Family Violence

Health and Wellness

Pathology is defined as the study of disease. However, before learning about disease, it is necessary to have a clear definition of health. In 1948, the World Health Organization defined health as "a state of complete physical, mental, and social well-being—not merely the absence of disease or infirmity." Almost 50 years later, *Stedman's Medical Dictionary for the Health Professions,* 7th edition, defines health as "a state characterized by anatomical, physiological, and psychological integrity, ability to perform personally valued family, work, and community roles; ability to deal with physical, biological, psychological and social stress; a feeling of well-being; and freedom from the risk of disease and untimely death." The definition and concept of health comprise a wide range of physical, emotional, and spiritual components.

The concept of health care has rapidly evolved over the past several decades, and many paradigms or models for health care have been examined and modified or eliminated. The role of the health care provider has changed from dictator to advisor and facilitator. The role of the patient has also changed. No longer do patients have to be passive participants; they can be dynamic partners in their own health care. The Internet has added a new dimension to the concept of access to health care information, enabling people to become informed consumers of health care if they so desire. People everywhere are looking at different methods of achieving "health" as it is defined today. They are seeing that many alternative and complementary forms of medicine have a place in the health care system. The concept of "wellness" places a strong focus on the active role of the patient and the importance of the total well-being of the person. The U.S. government has proposed four overarching goals in its 10-year agenda for improving the nation's health, *Healthy People 2020*. These goals are (1) attain high-quality, longer lives free of preventable disease, disability, injury, and premature death; (2) achieve health equity, eliminate disparities, and improve the health of all groups; (3) create social and physical environments that promote good health for all; and (4) promote quality of life, healthy development, and healthy behaviors across all life stages (Healthy People 2020, 2011). *Healthy People 2020* reflects the changing attitudes of Americans and encourages establishing a sense of personal responsibility as the key to good health. Students pursuing a career in health care study the healthy body in anatomy and physiology and other subjects throughout their formal education. This text draws on this knowledge extensively to provide a study of disease states.

Disease

Defining disease is far simpler than defining health. *Stedman's Medical Dictionary for the Dental Professions,* 2nd edition, defines disease as "an interruption, cessation, or disorder of a body, system, or organ structure or function," or "a morbid entity ordinarily characterized by two or more of the following criteria: recognized etiologic agent(s), identifiable group of signs and symptoms, or consistent anatomical alterations." The discussion of disease does not specifically refer to an infection with a microorganism; it includes any instance in which there is a change or alteration in **homeostasis,** or balance, within the systems of the body. Knowledge of the processes associated with disease is an essential part of the practice of dental hygiene. Dental hygienists must be aware of the impact disease has on the functioning of the human body.

The dental profession has known for years the mouth is not divorced from the rest of the body, but is an integral part of it. In the year 2000, the Surgeon General of the United States released "Oral Health in America: A Report of the Surgeon General." This report is the first of its kind, and its intent is to alert Americans to the full meaning of oral health and its importance to general health and well-being (USDHHS, 2000). Boxes 1.1 and 1.2 summarize the major findings of the report and the major functional and social implications of oral and craniofacial diseases that are identified in the report. What happens in the mouth can and does affect the rest of the body. Research, while not proving a causal relationship, appears to support the concept that periodontal infections may have an impact on the development, severity or progression of heart disease, stroke, diabetes, respiratory disease, and preterm

BOX 1.1

Major Findings of "Oral Health in America: A Report of the Surgeon General"

- Oral diseases and disorders in and of themselves affect health and well-being throughout life.
- Safe and effective measures exist to prevent the most common dental diseases—dental caries and periodontal diseases.
- Lifestyle behaviors that affect general health such as tobacco use, excessive alcohol use, and poor dietary choices affect oral and craniofacial health as well.
- There are profound and consequential oral health disparities within the U.S. population.
- More information is needed to improve America's oral health and eliminate health disparities.
- The mouth reflects general health and well-being.
- Oral diseases and conditions are associated with other health problems.
- Scientific research is key to further reduction in the burden of diseases and disorders that affect the face, mouth, and teeth.

From U.S. Department of Health and Human Services. Oral health in America: a report of the Surgeon General. Rockville, MD: U.S. Department of Health and Human Services, National Institute of Dental and Craniofacial Research, National Institutes of Health, 2000.

low-birth-weight babies. In addition, many pathologic conditions and diseases have oral manifestations that may appear in the early stages of the illness, possibly prior to any other symptoms. Although the importance of oral health in the context of total health is known by many, there are many more individuals who are not aware of the connection. Health care professionals, including dental health care professionals, are entrusted with the difficult task of helping patients to achieve and maintain an optimal state of health.

The Role of the Dental Hygienist

Eleven years after the Surgeon General's Oral Health in America Report, *Healthy People 2020* brings the role of the dental hygienist to the forefront of prevention again by setting goals to "increase the proportion of adults who receive preventive interventions in dental offices" (Healthy People 2020, 2011). Three goals specifically include the dental hygienist (in addition to the dentist) in the endeavor to (1) increase the number of adults receiving information or counseling in regard to tobacco cessation, (2) increase the number of adults receiving an oral and pharyngeal cancer screening, and (3) increase the number of adults being tested or referred for glycemic (blood sugar) control (Healthy People 2020, 2011). The dental hygienist is uniquely qualified, as the dental health care team's prevention specialist, to make observations regarding a patient's total health as it relates to oral health and vice versa. The dental hygienist is also in a position to develop strategies directed toward education and the early detection and prevention of disease. Patients schedule preventive appointments two to four times per year; therefore, the dental hygienist is in a key position to recognize abnormalities, sometimes before the patient even knows they exist, and to call attention to these abnormalities. Following collaboration with the dentist, the dental hygienist may be the person who assists the patient in obtaining the necessary care.

Objectives of the Clinical Evaluation

It is imperative each patient be thoroughly assessed for any indication of medical and/or oral problems prior to dental or dental hygiene procedures. The extraoral and intraoral examinations compose a large portion of this assessment, and while they are generally referred to as the extraoral and

BOX 1.2

Functional and Social Implications of Oral and Craniofacial Diseases as Reported in "Oral Health in America: A Report of the Surgeon General"

- Oral health is related to well-being and quality of life as measured along functional, psychosocial, and economic dimensions. Diet, nutrition, sleep, psychological status, social interaction, school, and work are affected by impaired oral and craniofacial health.
- Cultural values influence oral and craniofacial health and well-being and can play an important role in care utilization practices and in perpetuating acceptable oral health and facial norms.
- Oral and craniofacial diseases and their treatment place a burden on society in the form of lost days and years of productive work. Acute dental conditions contribute to a range of problems for employed adults, including restricted activity, bed days, and work loss, and school loss for children. In addition, conditions such as oral and pharyngeal cancers contribute to premature death and can be measured by years of life lost.
- Oral and craniofacial diseases and conditions contribute to compromised ability to bite, chew, and swallow foods; limitations in food selection; and poor nutrition. These conditions include tooth loss, diminished salivary functions, oral–facial pain conditions such as temporomandibular disorders, alterations in taste, and functional limitations of prosthetic replacements.
- Orofacial pain, as a symptom of untreated dental and oral problems and as a condition in and of itself, is a major source of diminished quality of life. It is associated with sleep deprivation, depression, and multiple adverse psychosocial outcomes.
- Self-reported impacts of oral conditions on social function include limitations in verbal and nonverbal communication, social interaction, and intimacy. Individuals with facial disfigurements due to craniofacial diseases and conditions and their treatments may experience loss of self-image and self-esteem, anxiety, depression, and social stigma; these in turn may limit educational, career, and marital opportunities and affect other social relations.
- Reduced oral-health-related quality of life is associated with poor clinical status and reduced access to care.

Taken from U.S. Department of Health and Human Services. Oral health in America: a report of the Surgeon General. Rockville, MD: U.S. Department of Health and Human Services, National Institute of Dental and Craniofacial Research, National Institutes of Health, 2000.

APPLICATION **1.1**

Oral Cancer Screening Examinations: Who Is Responsible?

Some dental health care professionals may believe the importance of the clinical evaluation is being overstated or the authors are overly passionate in their beliefs, but most hygienists will have the opportunity to save someone from disfiguring surgery or to save someone's life by performing a thorough cancer screening examination on each and every patient. Almost every year this author has been teaching dental hygiene, students or instructors have discovered an extraoral or intraoral suspicious lesion that has turned out to be malignant. For example, a student found a squamous cell carcinoma on her grandmother's arm. In another case, an instructor found a basal cell carcinoma at the corner of a student's eye during a preclinic demonstration of the extraoral examination. Also, a student was doing an extraoral examination on a relative and discovered a thyroid thickening that turned out to be a recurrence of thyroid cancer.

The dental hygienist is part of a team of individuals working to provide care and education for patients to help them achieve optimal oral and general health. Every person who examines a patient is important because what one misses, the others might not. Two separate studies, one by Alice Horowitz et al. and one by Jane Forrest et al., found that dental hygienists did not consistently provide oral cancer screening examinations for their patients even though most of them knew it should be done. Many stated such things as not having enough time or feeling inadequately trained as excuses for not providing this essential service (Horowitz et al., 2002; Forrest et al., 2001). In March 2004, Case Western Reserve University's School of Dental Medicine presented the results of a similar survey to the annual research meeting of the American Dental Education Association. They reported that although hygienists placed a high value on oral cancer screening, only 53% actually did the examinations on their patients. One notable finding was the level of knowledge about oral cancer, specifically the causes, appearance, and risk factors, among the dental hygienists surveyed was comparable to that of the general dentists surveyed 1 year earlier in 2003 (Cancer Weekly, May 11, 2004). A study of dentists and primary care physicians in Massachusetts by Applebaum et al. (2009) concluded there were gaps in oral cancer knowledge and practices indicating a need for more focused education in this area.

Rethman et al. (2010) reported there was sufficient evidence-based information to support oral cancer screening by visual and tactile methods as a means to detect cancer in the early stages. In 2009, Jennifer Watson et al. looked at a group of patients already diagnosed with oral or pharyngeal cancer to determine if oral/pharyngeal cancer screening examinations done in the primary care dental office were associated with early detection of the disease. They found that those patients who had a screening examination within the last year were significantly more likely to have an early-stage cancer than those who did not. A study of North Carolina dental hygienists by Carrie Bigelow et al. (2007) found hygienists play a key role in prevention not only in detecting precancerous and malignant lesions early but also in educating patients to avoid risk factors. Many patients are unaware they have had an oral cancer screening examination even when one has been performed. Almost 84% of patients surveyed by Sandra Johns and reported in the *Journal of Dental Hygiene* in Fall 2001 stated they had never had an extraoral examination (Johns, 2001). Other studies done by Scott Tomar et al. surveyed the oral cancer screening experiences of adult patients in Florida and the self-reported frequency of performing oral cancer screening examinations by dentists/dental hygienists in Florida. Less than 20% of adults over age 40 reported having a screening examination, while the dentists and hygienists reported they screened almost all of their patients over age 40. Obviously something is not right; either we are not performing the examinations or we are not telling our patients what we are doing and why. It is the dental professional's responsibility, our responsibility, to ensure patients receive: (1) appropriate and thorough assessment examinations, (2) appropriate follow-up and referrals, and (3) education informing the patient of their specific risks for oral cancer and other oral diseases. What will you choose to do during your professional career?

intraoral examinations, together they make up the oral cancer screening examination. Although these examinations may take less time to perform compared with a periodontal examination or a dental charting, they are extremely important. Information from the examinations is essential in determining if there is any indication of deviation from normal, not only in the oral cavity but also in the body as a whole. Findings may be suggestive of oral or pharyngeal cancer or of systemic conditions that may manifest in the oral cavity. The American Cancer Society estimates 61% of oral cancers are diagnosed at late stages, when regional and distant metastasis have already occurred (American Cancer Society, 2010). Late stage diagnoses complicate treatment and lead to low survival rates. The 5-year survival rate for all stages combined is 61%, with a range of 83% for localized lesions to 32% for distant metastasis (Howland et al., 2011). If more of these cancers were found at an earlier stage, survival rates would increase and morbidity (loss of function and disfigurement) would decrease. The American Cancer Society estimates 40,250 individuals in the United States will be diagnosed with oral or oropharyngeal cancer in 2012, and an estimated 7,850 will die from the disease in 2012 (American Cancer Society, 2012).

Positive findings during this examination can prompt the dental team to order additional tests or procedures to determine a diagnosis for the condition. The dental hygiene appointment may have to be postponed to obtain a medical consultation based on findings during this examination (see Box 1.3 for a listing of objectives of the clinical evaluation).

Some positive findings may cause the dental professional to suspect intentional trauma or neglect. (Refer to Application 1.5 at the end of this chapter and to Clinical

BOX 1.3 Objectives of the Clinical Evaluation

1. Screen for oral cancer
2. Determine whether the patient is well enough to continue dental treatment
3. Determine the need for medical or other consultations
4. Enable early diagnosis of pathology
5. Determine possible treatment modifications
6. Prepare and record baseline patient assessment information
7. Review and update baseline assessment information
8. Determine whether additional diagnostic procedures are necessary

Protocol 15 for more information on family violence and suggestions for recognizing and managing this situation.)

Performing an Extraoral Examination

The extraoral component of the examination should include a general assessment of the patient, an assessment of all visible areas of skin, and an assessment of the head and neck area. This assessment starts with the dental hygienist determining if there are any noticeable physical abnormalities as the patient walks to the dental chair. The patient's gait, posture, and how he or she sits in the chair should be observed as well as the patient's speech; any abnormalities should be noted in the patient's record. All visible areas of the patient's skin may be observed while gathering medical and dental history information and obtaining vital signs. Any abnormalities should be addressed using follow-up questions. The answers to these follow-up questions will determine the next course of action. Patients will respond to most questions that are asked in a professional manner, and most are very willing to discuss their physical status, especially when informed of the necessity for the information.

There is no set sequence for performing a head and neck examination; however, it should be done the same way every time. A systematic procedure for these examinations increases the amount of attention paid to what is being examined, instead of what should be examined next, and wondering if something was omitted. A systematic approach will also make the examinations faster and more reliable. Always look first (visual) and then palpate (tactile), pressing the tissue between fingers or against a firm structure such as bone in every area examined, even if there are no visible abnormalities. The head and neck area should be examined for symmetry by observing the patient from all angles including the supraorbital area (Fig. 1.1). The patient's profile should be classified as mesognathic, prognathic, or retrognathic. Observe the skin of the face, look for acne, moles (nevi), lumps or bumps, or roughened areas of skin. Many of the conditions or characteristics of conditions discussed in this text are referred to as **lesions**. A lesion is a wound or a distinct area in which a pathologic change has taken place. The more normal and abnormal entities the hygienist observes over time, the more observant he or she will become. With experience, the hygienist will see things that cause alarm as well as notice things that do not.

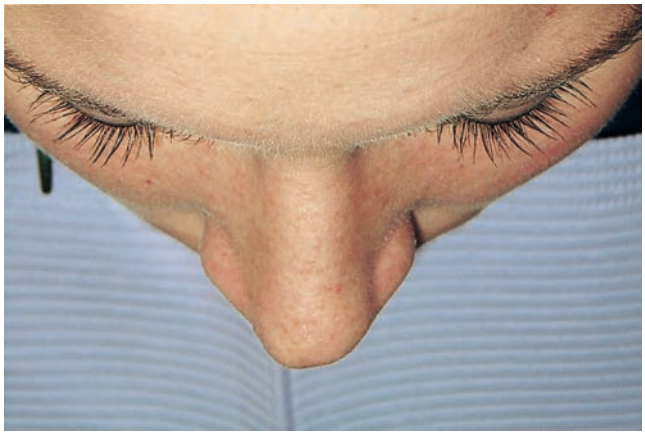

FIGURE 1.1. Supraorbital. Facial symmetry observed from the supraorbital aspect.

The following is a suggested order for performing the extraoral examination:

- Observe the eyes and the pupils. Figure 1.2 depicts an abnormal area at the inner canthus of the eye called a pterygium that may be caused by excessive exposure to sunlight or may be associated with lichen planus (see Chapter 14) or other skin disorders. This type of finding should be noted, and the patient should be questioned about it for a possible referral. Hold up the eyelids in older adults so the entire eyelid can be observed (Fig. 1.3).
- Look at the ears and the skin in back of the ears because patients are not able to see this area themselves, and it can be easily forgotten. Also check the area at the back of the neck, which can be observed while the lymph nodes are being palpated.
- Palpate the occipital, auricular, buccal, submandibular, submental, supraclavicular, and cervical chain, including the deep, superficial, and posterior lymph nodes. Figure 1.4 shows the locations of these lymph nodes. Findings that should be noted include **induration** or hardening, tenderness, mobility or movability, and, if abnormal, whether one or more nodes are involved. Another term used to

FIGURE 1.2. Pterygium. A pterygium is an overgrowth of tissue (conjunctiva).

FIGURE 1.3. Examine the upper eyelid. Stretch the upper eyelid so that you can observe all areas of the lid.

describe enlarged, indurated, and sometimes tender lymph nodes is **lymphadenopathy**. Figures 1.5 and 1.6 show clinically visible cervical lymphadenopathy.

- While palpating the nodes, be aware of the salivary glands in the area and extend the palpations to the parotid and under the mandible for the submandibular. Look for areas of swelling, induration, or tenderness.
- Examine the thyroid gland by pressing one side of the gland against the thyroid cartilage while holding the other side of the gland (Fig. 1.7). Then check to make sure the thyroid cartilage moves symmetrically during swallowing.
- Bilateral palpation of the temporomandibular joints should be done next. The function of the joint is best observed from a supraorbital position while the patient is opening and closing the mouth and moving the jaw from side to side (Fig. 1.8). In addition, examine the patient for any limitations in opening the mouth or for any joint sounds. Ask about joint tenderness or modifications in food choices made to accommodate painful joint function.

Any abnormalities should be accurately and completely recorded in the patient's record. Terminology and a suggested format for recording descriptions of abnormal conditions is presented following the discussion of the intraoral examination.

Performing an Intraoral Examination

The intraoral examination is a continuation of the extraoral examination and may overlap in several areas, especially

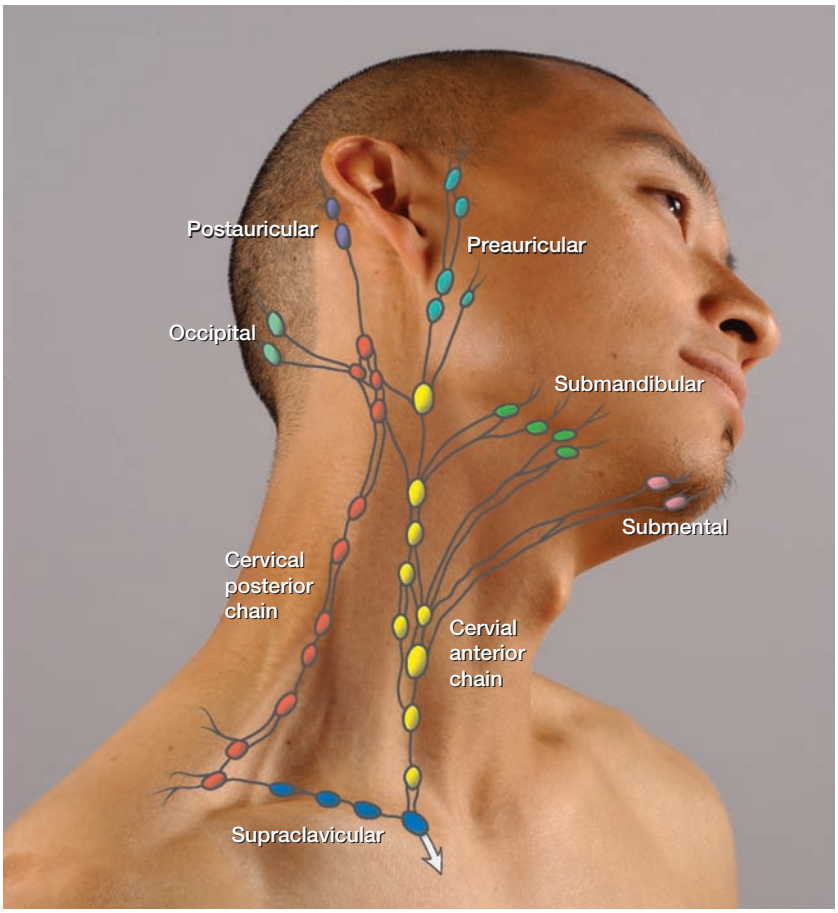

FIGURE 1.4. Lymph nodes of the head and neck. The location of the lymph nodes to be palpated during the extraoral examination. (From Nield-Gehrig JS. Patient assessment tutorials, 2nd ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins, 2010).

FIGURE 1.5. Lymphadenopathy. Clinically visible enlarged lymph node in anterior cervical chain. (Courtesy of Dr. Carolyn Bentley.)

near the lips and buccal mucosa. Again, the sequence of the examination is not as important as developing a routine, systematic approach. Repeating the same steps over and over again will increase the accuracy of the examination and decrease the chance anything will be missed. The following is a suggested sequence for performing the intraoral examination.

- The oropharynx is a common place to start. Make sure the entire area of the oropharynx is observed. There may be only one chance to see the area because some patients have a problem with gagging and after they realize what is being done they may become "difficult," even though they have been informed of the procedures prior to the start of the examination. Figure 1.9 depicts the oropharyngeal area of a patient who has a problem with the retention of food particles within the surface tissues of the tonsils. She complained of a bad mouth

FIGURE 1.6. Lymphadenopathy. Clinically visible enlarged lymph node in posterior cervical chain.

FIGURE 1.7. Examine the thyroid gland. Gently press the thyroid gland against the thyroid cartilage with the fingers of one hand while you hold the other side of the gland steady against the cartilage.

A

B

FIGURE 1.8. Examine the temporomandibular joint (TMJ). Position yourself to observe the mouth opening and closing and moving side to side from the supraorbital aspect while you bimanually palpate the TMJ. **A.** Opening and closing. **B.** Moving from side to side.

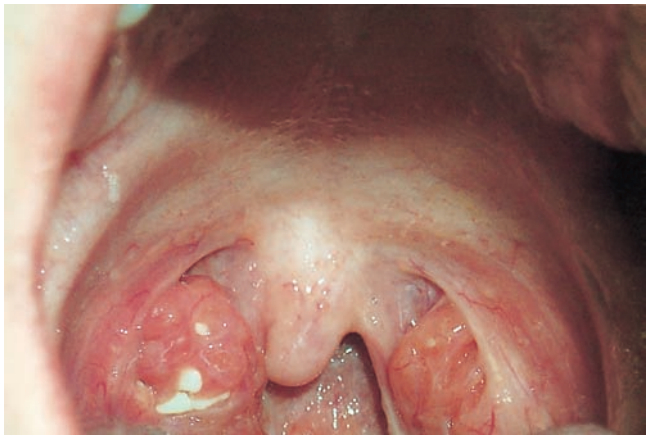

FIGURE 1.9. Examine the oropharynx. Get a good look at the entire oropharynx as quickly as possible. Notice the yellowish areas of food debris stuck in the craters of the tonsillar tissue.

FIGURE 1.11. Examine the floor of the mouth. Use the fingers of your intraoral hand to press the tissues of the floor of the mouth against the fingers of your extraoral hand.

odor and stated that occasionally she was able to remove the packed food from these areas with a toothbrush.

- Next, visualize and palpate the soft and hard palates and the maxillary tuberosity.
- Stretch out the buccal mucosa (Fig. 1.10) and roll the labial mucosa over your fingers and thumbs so you can visualize the entire surface of each. Palpate all of the soft tissues after they have been observed.
- Examine the mandible; stretch the alveolar mucosa at the floor of the mouth to see any areas that may be hiding under the inferior border of the mandible. Palpate the entire mandible from the inferior border to the angle of the mandible.
- Next examine the floor of the mouth; use bimanual palpation to press the structures against the fingers of your extraoral hand (Fig. 1.11). Look for any areas of color change, tenderness, induration, or masses.
- Hold the tongue with a gauze square and gently roll the tongue over on one side to observe the lateral border, then repeat for the other side (Fig. 1.12). Observe the dorsal and ventral surfaces and then palpate the entire tongue. After removing the gauze, observe the tip of the tongue.
- Finally, observe and palpate the attached gingiva on both the maxillary and mandibular arches.
- Assess the amount and quality of saliva by observation and by milking the parotid gland. Remember thick foamy saliva is usually a sign of a very dry mouth.
- Parafunctional habits such as bruxism (grinding) or clenching also need to be assessed and, if present, noted in the record.

Describing and Recording Clinical Findings

Written descriptions of an abnormality must provide enough detail so another professional the patient may need to see has enough information to decide whether the abnormality is resolving or becoming worse. Remember, the patient record is a legal document and should stand up to legal scrutiny if it ever becomes necessary. Intraoral photographs are being used in many practices to provide an adjunct to the written description for future comparison, but there must always be a written description in the

FIGURE 1.10. Examine the buccal mucosa. Stretch the buccal mucosa away from the maxillary and mandibular arches to examine the entire surface.

FIGURE 1.12. Examine the lateral borders of the tongue. Turn the tongue over rather than pulling the tongue out. It is not as uncomfortable and more can be seen than if the tongue is straight.

BOX 1.4

Observations which Might Indicate the Aggressiveness of a Particular Abnormality

1. Observations implying a more benign condition
   a. Nonulcerated lesions
   b. Bilateral involvement
   c. Sharply demarcated borders
   d. Multiple areas of involvement
   e. Elevated, soft, and movable lesions
   f. Lesions that have a direct cause and effect relationship
2. Observations implying a more aggressive, possibly malignant condition
   a. Paresthesia
   b. Single area of involvement
   c. Poorly defined and ragged borders
   d. Flat, indurated, and fixed lesions
   e. Alteration of the periodontal ligament space and/or lamina dura
   f. Mixed red and white lesions and velvety red lesions
   g. Lesions on the lateral borders of the tongue, soft palate, floor of the mouth, and lip
   h. Radiographic evidence of bone expansion or root erosion, displacement, or resorption

patient's record. Certain observations will cause the dental hygienist more concern than others. Some findings are often associated with very aggressive, **malignant** or cancerous conditions, while others may indicate relatively **benign** or noncancerous and less aggressive conditions. While these findings are often indicators of severity, do not be fooled into thinking this is always the case because even the most innocuous looking lesion may very well be malignant. Box 1.4 lists some observations that are associated with benign conditions and those that might imply a more serious or malignant condition. The description of unknown lesions or other abnormalities should include the following:

- History—Very often there is no history of an oral condition because the patient is unaware of having it. Sometimes the medical/dental history will provide clues to the etiology and history of the problem through notations about chronic conditions such as diabetes, recent illnesses, and medications. The patient should be asked about pain in the area or feelings of paresthesia (numbness, tingling, or other altered sensations). If there is pain, additional information such as the level of pain, whether it is sharp or dull, constant or occasional can help begin the process of determining what is happening.
- Location—An accurate description of the location of the lesion must be recorded. Some dental charts will have a diagrammatic representation of the areas in the mouth where a facsimile of the lesion can be drawn. If not, the location of the lesion needs to be described using appropriate terminology. Use terms such as inferior, superior, lateral, medial, anterior, posterior, distal, and mesial to denote location. Always try to pick a fixed point of reference close to the lesion to start the location description, such as adjacent to tooth 29 on the buccal mucosa or located in the middle one-third of the tongue, or 2 mm left of the midline. Use a probe to measure distances from the point of reference to the lesion and the size of the lesion itself.
- Distribution and definition—Terms that describe distribution include:
  - **Localized,** or found in one area only. The term "focal" can also be used (Fig. 1.13).
  - **Generalized,** or located in most of the tissues in one area. The term "diffuse" is also sometimes used (Fig. 1.14).
  - "Single lesion" (Fig. 1.13) or "multiple lesions" (Fig. 1.15) further define the distribution.
    - If there are multiple lesions, are they distinct or discrete and separate, or are they **coalescing** or growing together and becoming one large lesion (Fig. 1.16)?
  - Margins define the extent of the lesion and are either "well defined" or **circumscribed** (Fig. 1.17) or "poorly defined" and vague. Poorly defined margins are difficult to determine, and the dental hygienist may not be sure where the lesion ends and where normal tissue begins (Fig. 1.18).

FIGURE 1.13. Localized. This nodule is confined to the gingival tissues between the canine and the premolar.

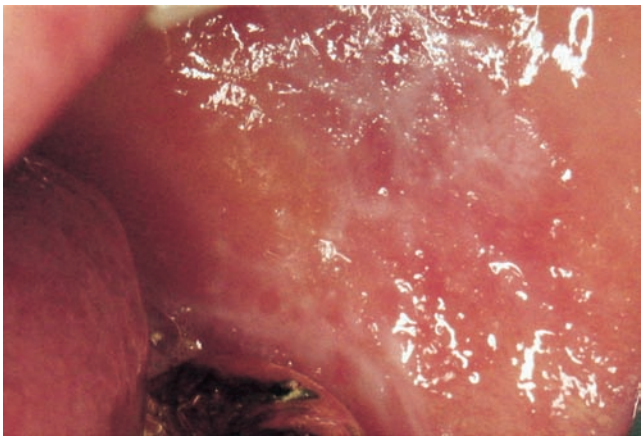

FIGURE 1.14. Generalized with irregular margins. This white lesion of lichen planus (see Chapter 14) called Wickham striae covers the entire right and left buccal mucosal surfaces with an irregular lacy pattern.

FIGURE 1.15. Multiple lesions. The hard palate is covered with multiple discrete lesions along with some that appear to coalesce.

FIGURE 1.16. Coalescing lesions. This recurrent herpes labialis lesion consists of separate vesicles that have begun to coalesce or grow together.

FIGURE 1.17. Well circumscribed with a well-defined regular margin. This granular cell tumor is well defined within the tissues. Note the yellow papules called Fordyce granules (see Chapter 14). (Courtesy of the U.S. Department of Veteran's Affairs.)

FIGURE 1.18. Poorly defined margin. Sun exposure has caused actinic keratosis or cheilitis on the lower lip. Some of the central areas are obvious, but it is difficult to determine exactly where the lesion ends, as it extends away from the central area. (Courtesy of the U.S. Department of Veteran's Affairs.)

- Well-defined margins may be "regular" (Fig. 1.17) or "irregular" (Fig. 1.24) in shape.

- Size and shape—Note the general shape and measure the size of the lesion with a probe. Measure the diameter of round lesions and the width and length of square, rectangular, and oval lesions. When writing the numbers for length and width, the width will come first; for example, a 5 inch by 7 inch frame will be 5 inches wide and 7 inches long. The size of a very large lesion might have to be related to the area it covers, such as the entire left lateral border of the tongue from the tip to the circumvallate papilla. If the lesion has any height, this must be noted also. Height is listed after the length of the lesion.
  - A flat lesion differentiated from the surrounding tissue by color alone is called a **macule** (Fig. 1.19) if it is less than 1 cm in diameter and a **patch** if it is more than 1 cm. A patch may also describe an area that has a different surface texture with or without a color change.

FIGURE 1.19. Macule. This flat lesion is differentiated from the surrounding tissue by color alone.

FIGURE 1.20. Vesicle. This recurrent herpes labialis lesion (see Chapter 11) is in the vesicular stage. The outlines of the smaller vesicles that have coalesced into this larger lesion are still visible.

- An elevated lesion may be a **vesicle** (Fig. 1.20) if it is 0.5 cm or less and is filled with a clear fluid. If it is larger than 0.5 cm, it would be called a **bulla** (Fig. 1.21).
- A **pustule** is a raised lesion filled with pus or **purulent exudate.**
- A raised lesion with no fluid inside is called a **papule** (Fig. 1.22) if it is less than 5 mm in diameter; a slightly larger, less than 2-cm, raised lesion is called a **nodule** (Fig. 1.23), and anything larger is called a **tumor.**
- If the area is broad, slightly raised, has a flat top, and looks pasted on, it is called a **plaque** (Fig. 1.24).
- A growth can be attached to the surrounding tissues by a broad or **sessile** base, as illustrated by the fibromas in Figures 1.22 and 1.23, or by a stalk (referred to as **pedunculated)** (Fig. 1.25).
- Depressed lesions can either be **ulcers** (Fig. 1.26), which extend through the epithelium into the dermis, or **erosions** (Fig. 1.27), which do not extend through the epithelium. Erosions can also be called **abrasions.**

FIGURE 1.21. Bulla. This large bulla formed as a result of a contact thermal burn.

FIGURE 1.22. Papule. This small fibroma (see Chapter 17) is the appropriate size to be described as a papule.

  - Two other terms are used to describe the general direction of growth of a lesion. **Exophytic** lesions grow outward from the surface of the tissue like the fibromas in Figures 1.22 and 1.23, and **endophytic** lesions grow into the surrounding tissues and present as palpable masses with or without any noticeable swelling.
- Color—Abnormal areas may be the same color as the surrounding tissues or they could be white, **erythematic** (red), yellow, or pigmented.
  - Normal color includes all variations of normal including normal physiologic pigmentations (Fig. 1.28).

FIGURE 1.23. Nodule. This larger fibroma on the buccal mucosa is considered to be a nodule.

FIGURE 1.24. Plaque. The slightly raised and flat configuration of this white lichen planus lesion covering a relatively broad area is indicative of a plaque. Also note the well-defined irregular margin.

- White lesions that cannot be wiped off (Fig. 1.24) usually involve excess keratin in the tissues, making them more opaque, like a callus on the hand.
- Erythematic areas (Fig. 1.29) usually indicate thinning of the epithelium allowing the more vascular subepithelial or submucosal tissues to be seen, or erythema

A

B

FIGURE 1.25. A, B. Pedunculated. The small pink papule apical to 24 and 25 **(A)** is attached to the underlying tissue by a thin stalk as seen when the tissue is lifted with the tip of an explorer **(B)**. (Courtesy of Dr. Harvey Kessler.)

FIGURE 1.26. Ulcer. These ulcers exhibit the classic features associated with this type of lesion, a central depressed area covered by a white pseudomembrane and surrounded by an erythematic ring.

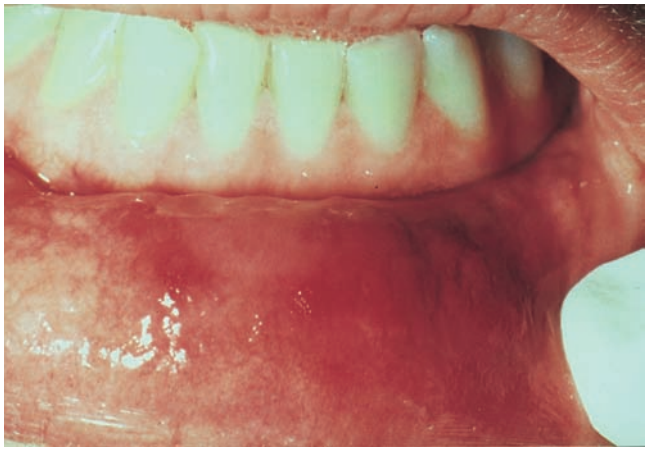

FIGURE 1.27. Erosion. Just the surface epithelium has been destroyed, leaving a diffuse area of erythema in these erosive lichen planus lesions on the lower lip.

FIGURE 1.28. Physiologic pigmentation. Normal melanin pigmentation of the gingival tissues.

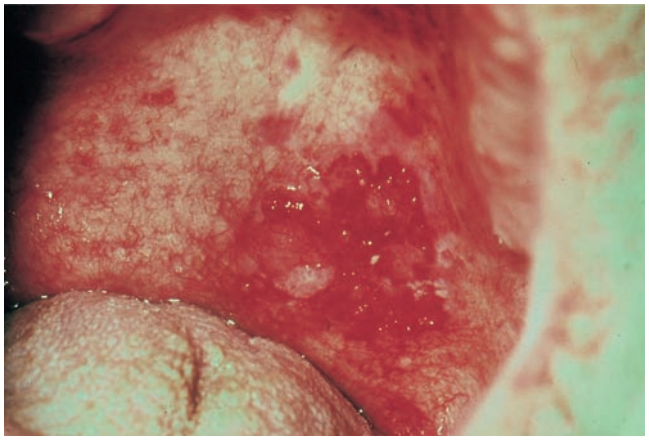

FIGURE 1.29. Erythema. This red lesion with poorly defined margins was found to be an invasive squamous cell carcinoma. (Courtesy of the U.S. Department of Veteran's Affairs.)

FIGURE 1.31. Black or blue/black lesion. An amalgam tattoo on the floor of the mouth. The amalgam was accidentally introduced into the soft tissues when an amalgam restoration was being placed. (Courtesy of Dr. Peter Jacobsen.)

may indicate an increased blood flow into the area due to an inflammatory reaction (see Chapter 3).

- Yellow can indicate the presence of purulent exudate or adipose tissue (fat) (Fig. 1.30).
- Other pigmentations include brown, black, and blue. These colors can represent either **endogenous** (from within the body) or **exogenous** (from an outside source) pigments. Black macules that are adjacent to teeth with amalgam restorations are very often caused by pigments from the amalgam, accidentally introduced into the soft tissues, leaching into the surrounding tissue, resulting in an **amalgam tattoo** (Fig. 1.31). Smaller black macules in the roof of the mouth, gingiva, or lips can be caused by a pencil lead being stabbed into the tissues. This is usually accidental and occurs when children run or play with a pencil in their mouth. The patient may or may not remember the incident. Another cause of a black macule is **melanoma,** a cancer of the pigment-producing cells or melanocytes (see Fig. 15.14A and B in Chapter 15). Melanoma is very serious and very difficult to treat. Blue lesions are most likely vascular, such as labial varicosities (Fig. 1.32) but they can also be intraoral nevi (Fig. 1.33) or melanomas. Brown lesions usually contain melanin pigments and can be associated with normal physiologic pigmentation, an intraoral nevus, a melanotic macule (Fig. 1.19), or a melanoma. Any black, blue, or brown pigmented lesion is cause for concern, and an explanation for its presence should be determined. The options for follow-up on lesions such as these are discussed in Chapters 5 and 15.
- Consistency—Consistency refers to how something feels when pressed on or between two surfaces such as between your thumb and forefinger or between your finger and the hard palate. Students and clinicians often confuse the terms used for consistency and those used

FIGURE 1.30. Yellow. Xanthelasma, a yellowish plaque located around the eye lids, is associated with high levels of cholesterol.

FIGURE 1.32. Labial varices. This older gentleman has a bluish vascular lesion on the upper lip.

FIGURE 1.33. Nevus. Blue nevus of the hard palate. (Courtesy of Marquette University School of Dentistry.)

for surface texture. Try to remember consistency is determined by how the area feels when pressed, not what it feels like when a fingertip is rubbed across its surface. Most of the case studies in this book provide a description of consistency, since consistency cannot be seen.

- The consistency of soft tissue abnormalities is often soft or normal feeling.
- Indurated soft tissue lesions, such as an inflamed lymph node, feel quite hard.
- **Fluctuant** is used to describe a fluid-filled lesion that moves fluid from one area to another when the lesion is pressed.
- Surface texture—The surface texture of an intraoral lesion is determined by how it feels when the pad of a fingertip is run across it and what it looks like. "Smooth" and "rough" are the main descriptive categories.
- A smooth surface texture is usually found when there is submucosal swelling and the surface of the lesion is covered by normal mucosal epithelium (Fig. 1.34).
- Rough surface textures are described by how they feel and how they look. Common terms to describe roughness include:
  - **Papillary,** consisting of finger-like projections (Fig. 1.35)
  - **Corrugated,** rippled, or washboard-like (Fig. 1.36)

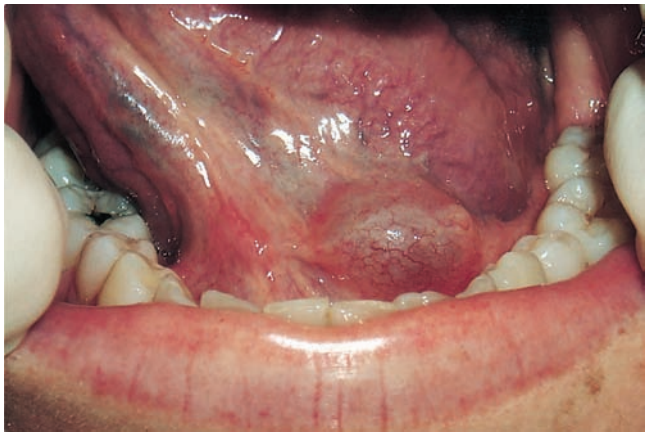

FIGURE 1.34. Smooth surface texture. The swelling on the floor of the mouth depicts a normal smooth surface texture.

FIGURE 1.35. Papillary. This lesion is made up of many finger-like projections as its name papilloma suggests. (Courtesy of the U.S. Department of Veteran's Affairs.)

FIGURE 1.36. Corrugated. The white corrugated lesions extending from the buccal mucosa through the mucobuccal fold up into the attached gingival are characteristic of those caused by spit tobacco use.

FIGURE 1.37. Fissured. This is a classic example of a fissured tongue. The deep fissures can collect food debris and provide a perfect environment for the growth of dental biofilm. The fissuring is not usually seen in children and worsens as the individual ages.

FIGURE 1.38. Pseudomembrane. The white surface membrane characteristic of pseudomembranous candidiasis leaves a sore erythematic area behind when it is wiped off with gauze.

- **Fissured,** consisting of many deep crevices (Fig. 1.37)
- **Crusted** or covered with a scab may also be used to describe perioral lesions (Fig. 1.16). The intraoral counterpart of a crust is a **pseudomembrane** or false membrane that covers the surface of a lesion and can be wiped off (Fig. 1.38).

Describing Radiographic Findings

Radiographs are an integral part of most dental examinations. Diagnostic radiographs may be exposed as part of a routine dental examination, or they may be exposed to obtain more information about an abnormality discovered through observation or palpation of the intraoral or perioral tissues. Radiographic abnormalities are often discovered by accident when there are no clinically observable signs or symptoms. A brief description of radiographic findings should be recorded in the patient's record in case the radiographs become misplaced. The features that should be described include the following:

- History—The patient should be asked whether he or she is aware of the area in the radiograph or not. If the patient is aware, ask what he or she was told it was, how long it has been present, and if there are any symptoms associated with it. The most common symptoms associated with bone lesions are pain and paresthesia. Very often there is no history, and the dental team will have to start the process of determining the cause of the lesion.
- Location and size—Determining the location of a radiographic finding is often made difficult by the radiographic technique used for exposing the film. Radiographs taken with excessive or inadequate vertical or horizontal angulation will not reflect the true location of the anomaly. Panoramic radiographs may also distort the true position of an anomaly. Care must be taken to use every means to accurately locate the abnormality. In most instances when there is doubt about the location, multiple radiographs will be taken from different aspects and with different angulations to more accurately place the anomaly. Size can be recorded in millimeters or centimeters and, if large, relative to the structures involved.
- Distribution—Distribution describes the number of anomalies and how they are positioned within the hard tissues.
  - "Single" is used to describe one lesion.
  - More than one lesion is described as "multiple lesions."
    - "Localized" or "focal" describes a clustered group of lesions.
    - "Generalized" or "diffuse" describes multiple findings in a large area of bone.
- Radiographic features—Specific terms are used to describe radiographic findings. These terms include the following:
  - Whether a radiographic anomaly is **radiopaque** (whiter than the normal radiographic appearance of the bone) as in Figure 1.39, **radiolucent** (darker than the normal radiographic appearance of bone) as in Figure 1.40, or **mixed** (consisting of both radiopaque and radiolucent areas) as in Figure 1.41 will help to exclude many conditions from a list of potential diagnoses. The radicular cyst (see Chapter 20) seen in Figure 1.40 would not be considered as a possible

APPLICATION **1.2**

Clinical Description of Oral and Perioral Lesions

Refer to Figure 1.34 for an image of the soft tissue description developed in this section.

History: The patient was unaware of this lesion until 2 days ago. She reports no history of trauma, and there are no significant findings on the medical or dental histories.

- Location: Floor of the mouth (FOM) 5 mm to the left of the lingual frenum at the level of the sublingual caruncle
- Distribution and definition: Single, localized, and well circumscribed
- Size and shape: Round nodule 18 mm in diameter 10 mm in height, sessile base
- Color: Slightly bluish with an erythematic ring around the base
- Consistency: Soft and fluctuant
- Surface texture: Smooth

Description: Single, well-circumscribed, bluish nodule approximately 18 mm in diameter and 10 mm in height, surrounded by an erythematic ring, soft, fluctuant with a smooth surface and sessile base, located on the FOM, 5 mm left of lingual frenum level with sublingual caruncle. Patient reports she became aware of the swelling 2 days ago, no report of trauma, no other significant findings on the medical or dental histories.

FIGURE 1.39. Radiopaque. Note the well-defined radiopaque area of condensing osteitis at the apex of the root of the second premolar and first molar.

diagnosis if the spherical lesion at the apex of a tooth were radiopaque. Condensing osteitis (see Chapter 19) would be much more likely because its normal presentation is radiopaque (Fig. 1.39), while that of a radicular cyst is radiolucent.

- Many lesions present as a single or **unilocular** radiopaque or radiolucent area, while others look as if there are compartments within the lesion. A radiolucent lesion made up of these compartments is said to be **multilocular,** and they are often described as having a "soap bubble" appearance (Fig. 1.42).
- It is important to determine the clarity of the margins of a radiographic anomaly. Lesions with clearly defined or well-demarcated margins (Fig. 1.43) are more likely to be benign and less aggressive entities. Indistinct margins should be described as poorly defined or "irregular." Poorly defined margins will appear fuzzy or ragged, and it is difficult to determine

FIGURE 1.40. Radiolucent. Note the well-defined spherical radiolucent area apical to the canine.

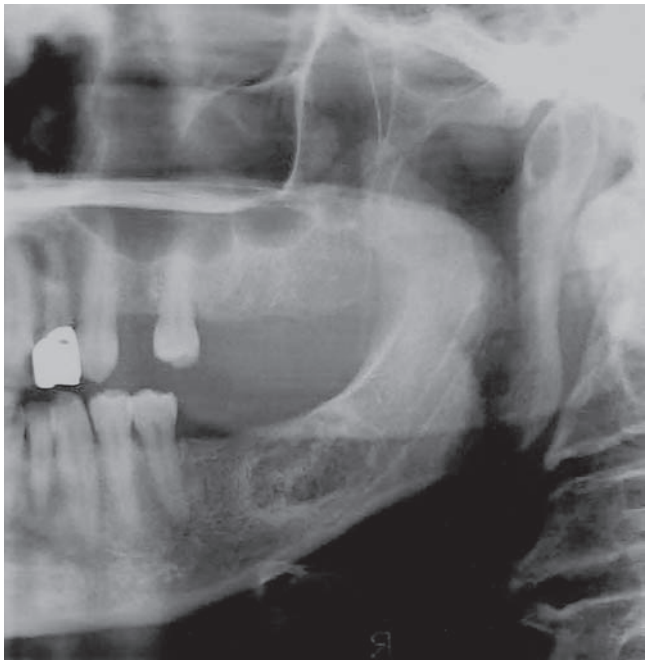

FIGURE 1.41. Mixed. This lesion exhibits both radiolucent and radiopaque characteristics.

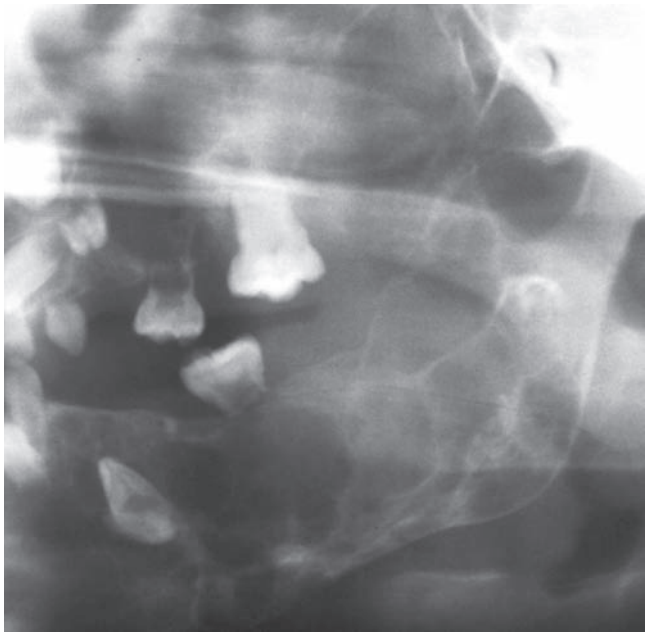

FIGURE 1.42. Multilocular. The multilocular radiolucent lesions in this radiograph are associated with a connective tissue condition called cherubism.

FIGURE 1.43. Well-defined margins. The odontoma (see Chapter 19) is an example of a lesion that has well-defined radiographic margins as well as mixed radiolucent and opaque elements.

FIGURE 1.45. Root resorption. The distal root of the mandibular second molar has been severely resorbed by the pathologic lesion surrounding the unerupted third molar.

where the abnormal hard tissue ends and the normal tissue begins (Fig. 1.44). Poorly defined margins are considered to be more indicative of an aggressive or malignant condition.

- The appearance of the surrounding tissues is also important, and close attention must be paid to this area.
  - If the abnormality involves the roots of any teeth, it is important to determine if it is causing **resorption** or destruction of the roots (Fig. 1.45) or causing them to move out of the way through **convergence**

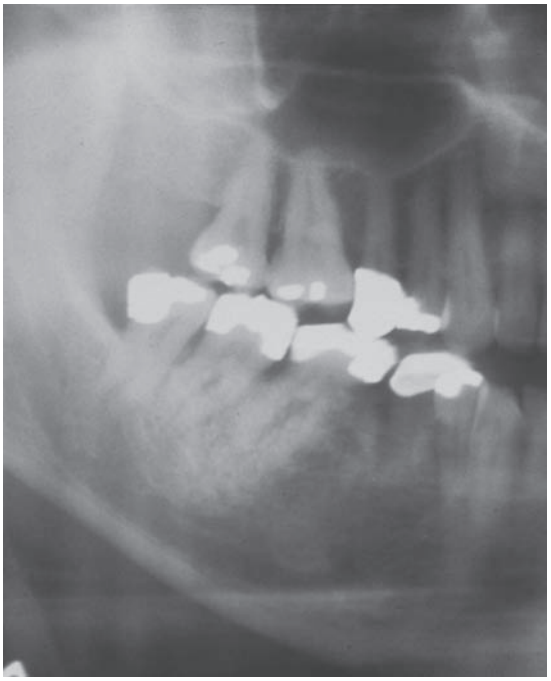

FIGURE 1.44. Poorly defined margins. Note the radiopaque area surrounding the first and second molars and the slightly opaque areas that seem to be extending toward the anterior region. It is difficult to determine the extent of this osteogenic sarcoma (bone cancer) because of the poorly defined borders. (Courtesy of the U.S. Department of Veteran's Affairs.)

FIGURE 1.46. Divergence. This radiolucent lesion has caused the canine and lateral roots to spread apart.

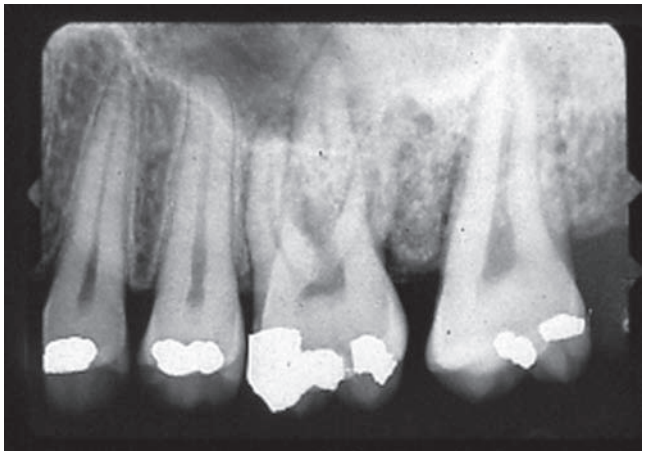

FIGURE 1.47. Widening of the periodontal ligament space. This radiograph is of a 34-year-old woman who was incorrectly treated for periodontal disease. Note the widened periodontal ligament space around the first molar. There is a separation between the first and second molar, and the interproximal alveolar bone has a mottled atypical appearance compared to what would be expected. A biopsy of the area between the two molars found osteogenic carcinoma. (Courtesy of Dr. John W. Preece.)

(movement toward each other) or **divergence** (movement away from each other) (Fig. 1.46).

- Changes in the periodontal ligament space such as widening (Fig. 1.47) or loss of the space should be noted.
- The lamina dura should be observed to determine whether there have been any changes in its structure or if it is missing altogether.
- If the cortical bone can be seen, it should be noted if there have been any changes, specifically if the lesion has been able to erode through the cortical bone (Fig. 1.48) or if there has been expansion of the bone in the surrounding area (Fig. 1.49).

Determining a Diagnosis

Creating a differential diagnosis for a particular lesion can be very interesting and educational. Exploring the outermost boundaries of the scope of dental hygiene practice can provide intellectual stimulation and create career satisfaction.

Differential Diagnosis

A **differential diagnosis** is a listing of the probable causes of a particular disease manifestation or group of manifestations. There is a process involved with creating a differential diagnosis, and it should be followed more or less every time something is seen that cannot be identified. The steps to creating a differential diagnosis are as follows:

1. Describe the abnormality in clinical terms.
2. Determine a list of diseases/conditions that present with similar manifestations.
3. Eliminate some of the possible causes already listed by adding other factors that could be involved with the

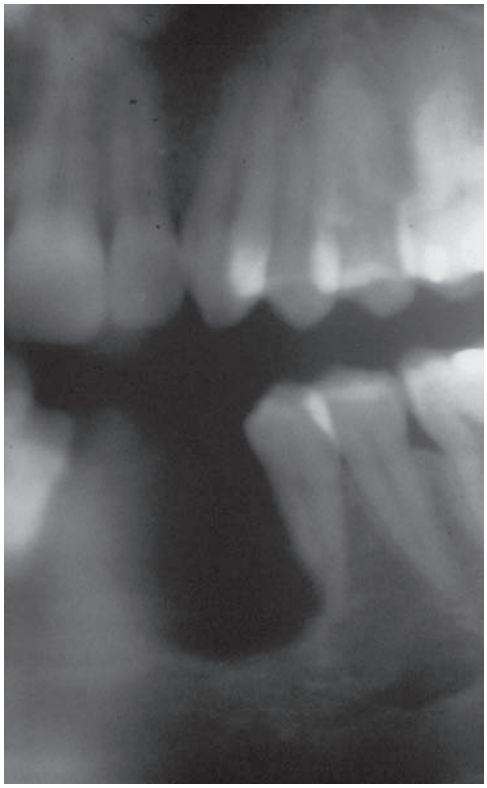

FIGURE 1.48. Cortical bone destruction. The central giant cell granuloma (see Chapter 18) pictured in this radiograph has eroded through the cortical bone in the edentulous mandibular area. (Courtesy of the U.S. Department of Veteran's Affairs.)

abnormality (chronic health condition, medications, patient age, and whether the patient has any other manifestations that are inconsistent with any of the listed possibilities).

4. Rank the remaining possible causes according to the probability they are the causative agent.
5. Decide what additional information might be necessary to eliminate more of the possibilities, such as blood

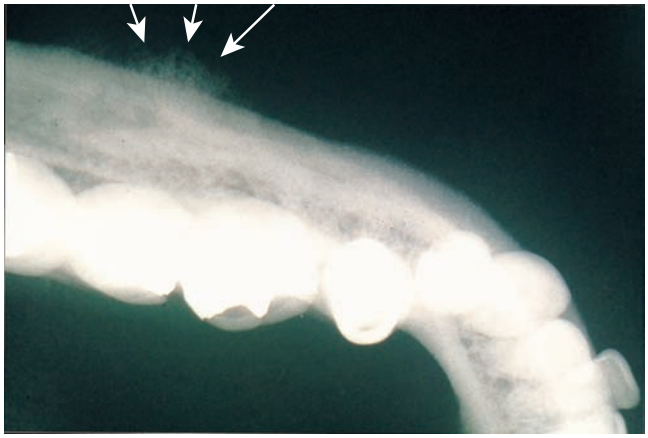

FIGURE 1.49. Bone expansion. This is an occlusal view of an osteogenic sarcoma (see Chapter 18). Note the sunburst pattern of abnormal bone and expansion that are characteristic of this tumor. (Courtesy of the U.S. Department of Veteran's Affairs.)

APPLICATION **1.3**

Radiographic Descriptions

The panoramic radiograph in Figure 1.50 depicts the radiopaque object used as the example for developing the following radiographic description.

- Location: Left ramus of the mandible just inferior to the condyloid process
- Size: Round, approximately 1 cm in diameter (in the original film)
- Distribution: Single
- Margins: Well defined
- Opacity: Radiopaque

Description: A single, well-defined, 1-cm diameter, round radiopaque object located slightly inferior to the left condyloid process.

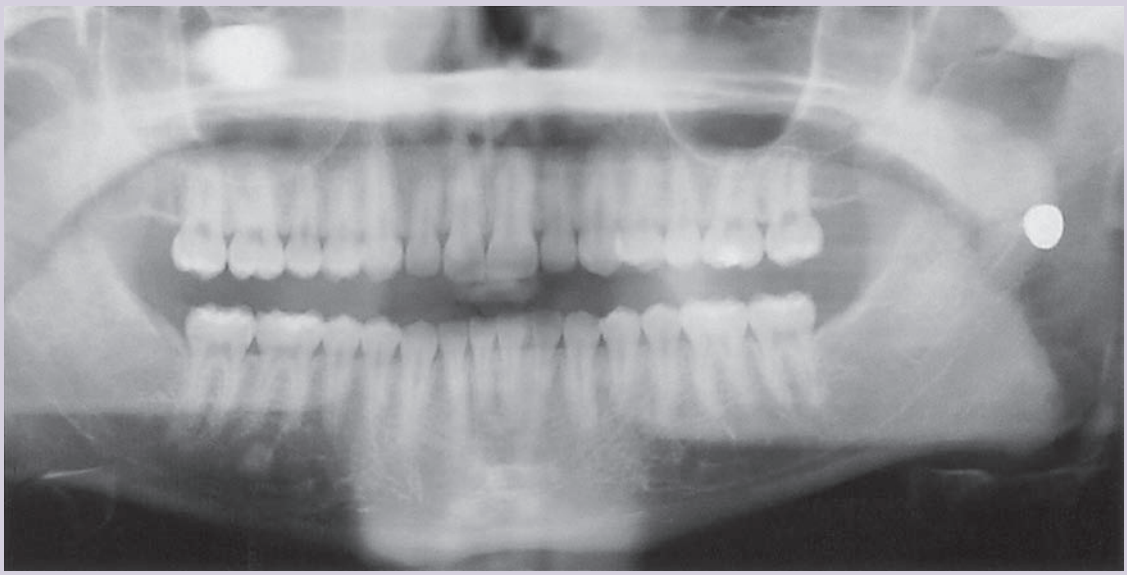

FIGURE 1.50. Radiopaque object.

tests, **biopsy,** diagnostic radiographs, cultures of oral microbes, and medical consultations.

The clinician may decide to treat the lesion as the manifestation of the most likely cause as the best course of action (therapeutic diagnosis). For example, if the most likely cause of a lesion is a fungal infection, and it is treated for 10 days with a topical antifungal medication resolving the lesion, it was most likely a fungal infection. A second possibility is that it resolved on its own, and no one will ever be sure of the actual cause. If it does not resolve, more specific diagnostic procedures are appropriate. It is not within the scope of practice of a dental hygienist to order any of these tests or to recommend some therapies, but it is appropriate to be aware of what the options are and thus be able to have some input as a valuable member of the dental team. If a definitive diagnosis is not determined by the additional information obtained, then the list of conditions that remains is the differential diagnosis.

Definitive Diagnosis

A **definitive diagnosis** is determined when all of the suspected causes on the list except one have been eliminated. That one cause is the definitive diagnosis. It would be difficult for the dental hygienist to repeat this process every time an abnormal area in or around the oral cavity was discovered. Fortunately, such a lengthy process is not necessary. Many of the most common abnormalities have such distinguishing characteristics that unlikely causes can be eliminated solely through observation of the abnormality. Some of the conditions discussed in this book are **atypical,** or variations of normal, and not pathologic. By observing these conditions clinically, the dental hygienist will become very familiar with them and will know immediately if there is something else happening. Conditions such as leukoedema and tori can be clinically diagnosed because they are very common and have such clear clinical manifestations there is no doubt about what they are. Some other pathologic conditions such as caries can be diagnosed from their characteristic radiographic appearance. The danger arises when the dental team starts assuming everything seen is a variation of normal. Often, there is concern the patient might be subjected to undue stress about something that is most likely benign. An effort must be made to determine the cause of all suspicious areas identified. In many cases, this will require a visit to an oral surgeon for a biopsy; or the biopsy, exfoliative cytology, or brush biopsy may be performed in the general dental office.

APPLICATION **1.4**

How to Create a Differential Diagnosis

The following is a simple example of how to create a differential diagnosis. The possible causes listed in the differential diagnosis are described in detail in Chapter 12. Refer to this chapter if necessary for a more complete description of why a condition is eliminated from the list of possibilities. Refer to Figure 1.51 for this application.

FIGURE 1.51. Differential diagnosis.

1. Clinical description and history: Single, well-defined ulcer covered by a white pseudomembrane and surrounded by an erythematic ring; the ulcer is oval, approximately 4 mm × 3 mm, firm and slightly rough to the touch, located on the lower labial mucosa adjacent to tooth 27 at the margin of the labial mucosa and the extraoral lip tissue. The patient is 10 years old and has no significant medical or dental findings other than the report of slight pain in the lip.
2. The following are considered as part of the differential diagnosis:
   - Reiter syndrome (Chapter 12)
   - Syphilis (Chapter 12)
   - Erythema multiforme (Chapter 12)
   - Traumatic ulcer (Chapter 12)
   - Recurrent aphthous ulcer (Chapter 12)
3. Rationale for excluding some elements of the differential diagnosis
   - Reiter syndrome usually occurs in males in their 30s and normally manifests with concurrent generalized arthritis. This young man is 10 and reports no significant medical findings such as arthritis. Thus, Reiter syndrome can be eliminated as a possibility.
   - Primary syphilis is a sexually transmitted disease that presents with a large ulcer-like chancre at the initial point of contact. This patient is most likely not sexually active at age 10, but the possibility of sexual abuse would have to be ruled out. The clinical appearance of this lesion is much too small to be a chancre, and there would be no pain associated with a chancre, so this can also be eliminated.
   - Erythema multiforme is an immune response that presents with skin and mucous membrane lesions. The absence of skin lesions and the fact that this is a solitary lesion probably indicate that this disorder can be eliminated.
   - Traumatic ulcers look like this lesion, and they are often found on the lip, tongue, cheeks, and other areas that are subject to frequent trauma. This diagnosis is highly likely.
   - Recurrent aphthous ulcers look like this lesion and present on the moveable mucosa; in addition, they can be precipitated by trauma to the tissues. It is not known whether this patient has had this type of ulcer before. Without more information, this diagnosis must also be considered likely.
4. A ranking of the remaining possibilities is difficult in this case because there is an equal probability it could be either one. In this case, more information is needed. It is necessary to ask a few more questions, such as the following:
   - When did you notice the ulcer?
     - Answer: About 2 days ago.
   - Have you ever had ulcers like this on your lip or in your mouth before?
     - Answer: I had one on my gums after I hit myself with a toothbrush.
   - Do you remember doing anything to cause the ulcer?
     - Answer: Yeah, I bit my lip!
5. These questions have clarified the circumstances that occurred prior to the development of the ulcer. The following must be considered before eliminating either of the possibilities.
   - Only one other ulcer located on the attached gingival surface occurred previous to this ulcer, and that ulcer was also associated with trauma.
   - Recurrent aphthous ulcers do not normally affect the attached gingiva, indicating that the previous ulcer was probably not recurrent aphthous.
   - Causal relationships are important, and in this case the patient has supplied the cause.
6. The only possible way to obtain a definitive diagnosis of this lesion would be to biopsy the lesion, which may not provide anything more than to describe the lesion as containing inflammatory cells, which would be likely in either case. The cause-and-effect relationship between the trauma of biting the lip and the appearance of the ulcer and the fact that there is no previous report of aphthous ulcers support the diagnosis of a traumatic ulcer. The clinical manifestation of the ulcer would be treated the same way for either diagnosis. The only consideration would be to alert the patient of the possibility that more ulcers occurring in the absence of trauma might indicate recurrent aphthous ulcers.

APPLICATION **1.5**

Family Violence: Recognition and Appropriate Intervention

The epidemic of family violence (the abuse or neglect of children, adults, or the elderly) continues to grow in the United States and elsewhere with as many as 10 million victims each year in the United States alone. The dental team faces two challenges in dealing with the full spectrum of family violence: (1) the magnitude of the family violence problem and (2) the apparent lack of involvement from dental professionals. The size of the family violence epidemic is constantly growing, but is difficult to measure. Recent statistics have shown that the incidence of child abuse and neglect, the only universally reportable forms of family violence, continues to rise. Typical data show as many as 3 million children each year are reported to child protective service (CPS) agencies in the United States.[1] Moreover, as many as 2,000 children are fatalities of abuse and neglect each year.[1]

The incidence of intimate partner violence (IPV)* and elderly abuse is even larger, although difficult to quantify. Estimates from various sources show that these forms of family violence are as pervasive as child maltreatment. Elderly abuse is at least as common as child abuse and IPV is more common than child abuse.[2,3] Dr. Donna Shalala, former U.S. Secretary of Health and Human Services, has put the magnitude of the IPV epidemic into perspective by stating that it is "as common as birth in the U.S., four million occurrences each year."

Obviously, the size and seriousness of these epidemics is staggering, but dentistry's major involvement has traditionally focused on child abuse and neglect. However, dentistry's commitment to preventing child maltreatment is not commensurate with the epidemic. Although as much as 75% of child abuse injuries occur to the head, neck, and face, few dentists apparently ever recognize or report a case of child maltreatment.[4] A protocol for helping professionals identify family violence will most certainly ameliorate this discrepancy as it relates to victims of any age.

Identification

Many of the steps in identifying family violence are applicable for victims of any age. It is imperative to note that safety planning must be a consideration for any possible family violence intervention. Safety planning must include protocols to maintain confidentiality for victims, procedures for summoning the police or other emergency aid to the office, and plans for how to protect both victims and office staff from violence. Literature about community resources that are available to help victims should be made available. This information could be discretely placed in the ladies' restroom as opposed to the reception area. A victim may be more comfortable reading or taking this information while she is in the privacy of the ladies' room.

Even though the potential for violence within the dental office is minimal, understand that perpetrators might want to stop interventions on behalf of the victim. Every office should have a "safe room." A safe room must have a sturdy door that can be locked from the inside, have an outside telephone line, and be large enough for the staff and patient to remain in until help arrives.

Recognizing family violence can be facilitated by following a simple protocol (Table 1.1). Start by doing a general physical assessment of the patient. While a physical examination is not appropriate in all health care settings, the practitioner can always observe the patient for signs that may be consistent with trauma, or show obvious delay in seeking treatment. A patient's behavior may also indicate a history of violence. While everyone's behavior is unique, patients tend to behave differently in the clinical setting than outside this environment, and certain behaviors may lead one to suspect violence. Judge your patient's behavior in light of their maturity and the current setting (Clinical Protocol #15).

All patients undergo a health history that is updated at each appointment. Especially when dealing with children, it may be useful to get one history from the adult and another, in a separate setting, from the child. Histories about an injury that do not match may indicate violence. Separate dual histories may also be important when dealing with adults or the elderly since victims will often not answer honestly in the presence of the perpetrator.

Examination of the oral cavity and surrounding structures can identify signs of family violence including injuries to the teeth and supporting structures. Perioral lesions including lacerations, contusions, pattern injuries, or oral lesions of sexually transmitted diseases may also indicate family violence (Figs. 1.52–1.54).

In some cases, it may be useful to consult with the patient's physician. Confidential consultation between health care professionals is important for a variety of conditions, and family violence suspicions can be strengthened or alleviated by this personal contact.

Appropriate Intervention

When a health care provider makes the decision to intervene in suspected family violence situations, one must take action appropriate to the age of the victim, the situation, and the statutory requirements. Health care providers in all states are required to report suspected cases of child abuse or neglect, consistent with state law. Carefully document physical and behavioral indicators of abuse or neglect in the patient's chart. Also report, verbatim, statements of history when the histories do not match. It is useful to have a witness in the operatory during the child's examination and history, and that person should cosign the child's chart.

Call the appropriate CPSs agency for your jurisdiction. Reporting agencies are specific to states and counties and may include not only social service agencies but also law enforcement agencies. Be sure to know your reporting

*Note that the term "intimate partner violence" is the current terminology for what has previously been known as "domestic violence" or "spousal abuse." Also note that some states' statutory language uses "domestic violence" when they mean the problem affecting victims of any age.

TABLE 1.1 **Physical and Behavioral Indicators of Abuse and Neglect**

Type of Child Abuse/Neglect	Physical Indicators	Behavioral Indicators

Physical Abuse	*Unexplained Bruises and Welts:*
	■ Face, lips, mouth
	■ Torso, back, buttocks, thighs
	■ Various stages of healing
	■ Clustered, regular patterns
	■ Reflecting shape of article used to inflict (e.g., buckle)
	■ On several different areas
	■ Regular appearance after absence, weekend, vacation
	Unexplained Burns:
	■ Cigarette, cigar burns, esp. on soles, palms, back, buttocks
	■ Immersion burns (sock or glove-like, circular, on buttocks or genitalia)
	■ Patterned: electric burner, iron
	■ Rope burns on arms, legs, or torso
	Unexplained Fractures:
	■ Skull, nose, facial structures
	■ In various stages of healing
	■ Multiple or spiral fractures
	Unexplained Laceration or Abrasion:
	■ To mouth, lips, gingiva, eyes
	■ To external genitalia
		■ Wary of adult contacts
		■ Apprehensive when others cry
		■ Behavioral extremes:
		  ■ Aggressive
		  ■ Withdrawn
		■ Frightened of parents
		■ Afraid to go home
		■ Reports injury by parents

Physical Neglect	■ Constant hunger, poor hygiene, inappropriate dress ■ Consistent lack of supervision, esp. in dangerous situations or for long periods ■ Unattended physical problems or medical/dental needs ■ Abandonment	■ Begging, stealing food ■ Extended stays at school, early arrival, late departure ■ Constant fatigue, falling asleep in class ■ Alcohol or drug abuse ■ Delinquency (e.g., thefts) ■ Says there is no caretaker
Sexual Abuse	■ Difficulty in walking or sitting ■ Torn, stained, bloody underwear ■ Pain or itching in genital area ■ Bruises or bleeding on external genitalia, vaginal, or anal areas ■ Venereal disease, esp. in preteen ■ Pregnancy	■ Unwilling to change for PE ■ Withdrawal, fantasy, or infantile behavior ■ Bizarre, sophisticated sexual knowledge or behavior ■ Poor peer relationship ■ Delinquency; runaways ■ Reports sexual assault by caretaker

Emotional Maltreatment	■ Speech disorders
	■ Lags in physical development
	■ Failure to thrive
		■ Habit disorders (sucking, biting, rocking, etc.)
		■ Conduct disorders (antisocial, destructive)
		■ Neurotic traits (sleep disorders, inhibited play)
		■ Psychoneurotic behaviors (hysteria, phobia, obsession, compulsion, hypochondria)
		■ Behavior extremes:
		  ■ Compliant, passive
		  ■ Aggressive, demanding
		■ Overly adaptive behavior:
		  ■ Inappropriately adult
		  ■ Inappropriately infantile
		■ Developmental lags (physical or mental)
		  ■ Attempted suicide

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(continued)

APPLICATION 1.5 *(continued)*

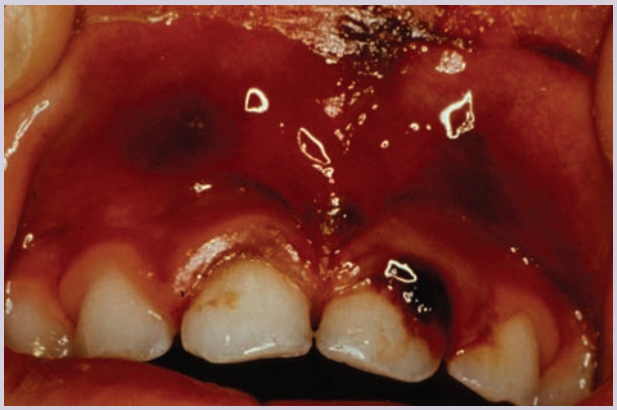

FIGURE 1.52. Family violence. Multiple oral injuries, including lacerated lip, torn frenum, bruised vestibular tissue, and subluxated central incisor, all caused by an open-handed slap. (Courtesy of Lynn Douglas Mouden.)

requirements and keep the reporting number easily available. The person taking information will guide the reporting process and ask for identifying information. That information may include the child's name and address, age, siblings, the nature of the current condition, and other useful information including the name of the suspected perpetrator. While in some jurisdictions reports can be accepted from anonymous sources, health care professionals should identify themselves so that follow-up inquiries are possible when necessary.

When providing assistance for adult or elderly victims, one must also know the statutory requirements specific to the jurisdiction. State laws on reporting adult and elderly victims of family violence vary widely and must be understood prior to the situation arising. Remember that the patient's health and safety must be your first concern and inappropriate intervention, or reporting when not required, may actually place the patient at higher risk.

When dealing with adult victims, health care professionals must learn that their role is to serve as facilitators providing

FIGURE 1.53. Family violence. Condyloma acuminatum (venereal warts) contracted during an oral rape. (Courtesy of Lynn Douglas Mouden.)

FIGURE 1.54. Dental neglect. Untreated gross caries with multiple draining abscesses. (Courtesy of Lynn Douglas Mouden.)

information, support, and encouragement. Therefore, providers must learn to communicate respect for all their patients, support their patients' decisions, and be knowledgeable about available community resources. Provide adult victims the opportunity and resources to change their lives. Every health care provider must develop attitudes that will allow them to assist all victims of family violence such as attitudes of urgency, respect, concern, and community.

The Dental Profession's Response to the Problem

Several initiatives in recent years have helped health care professionals and others deal with family violence. The most notable program is the Prevent Abuse and Neglect through Dental Awareness (P.A.N.D.A.) Coalition. P.A.N.D.A., which began with the model program in Missouri, is now in place in 46 U.S. states and 14 international coalitions. Individuals in the remaining U.S. states and many countries are working to form the public/private partnerships that make the P.A.N.D.A. program work. Putting together the resources of health care, education, public health, insurers, and social services has been the key to the program's effectiveness. Not only is the dental profession more aware of the problems of family violence in P.A.N.D.A. states, these coalitions have proven their effectiveness. P.A.N.D.A. has shown notable success. Although nationally the total reports of suspected child abuse and neglect have continued to rise approximately 6% each year, following the first year of P.A.N.D.A.'s educational and awareness campaign in Missouri, the number of reports made by dentists rose by 60%.[5] After 4 years of the P.A.N.D.A. program, the reporting rate by dentists has now risen by 160%.[6] In Illinois, the reporting rate rose an astounding 800% after 5 years of the P.A.N.D.A. program.

Every health care professional must understand not only the symptoms of family violence, but also be familiar with local resources to help stop the violence. Every professional must take steps to deal with suspected victims: (1) know and understand the applicable state, tribal, or federal laws; (2) learn what is available to help victims in your own community; (3) get involved with P.A.N.D.A. or similar programs; (4) seek out educational opportunities to prepare yourself; and, most

APPLICATION 1.5 *(continued)*

importantly, (5) show concern for every patient's total health and demonstrate your willingness to help. Remember that victims of family violence fall into only two categories, those who survive and those who do not.

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This section was written by Lynn Douglas Mouden, DDS, MPH, FICD, FACD. Dr. Mouden is Director, Office of Oral Health in the Arkansas Department of Health and is a founder of the P.A.N.D.A. program. For more information, you may contact Dr. Mouden at 501-661-2595 or Lynn.Mouden@arkansas.gov.

Some patients may be unduly alarmed by a referral for a biopsy of what turns out to be an amalgam tattoo, but the alternative diagnosis of a melanoma must be considered until ruled out. Many of the conditions throughout this book include a differential diagnosis or listing of other conditions that may cause similar lesions. Attention should be paid to these and they should be incorporated into the student's dental hygiene education.

SUMMARY

- The concept of health comprises a wide range of physical, emotional, and spiritual components.
- Individuals are being encouraged to take charge of their lives and establish a sense of personal responsibility for their own health.
- Patients are expected to take a dynamic role in their health care. Health care providers are not only expected to provide treatment but also to facilitate this new active role by helping to direct and educate the patient in ways of attaining total body wellness.
- Oral health is an integral part of total body health, and the dental team is responsible for helping the patient achieve and maintain good oral health.
- The oral cancer screening examination is an important element in determining the oral health of the patient. Oral cancers are usually diagnosed in the late stages, and early diagnosis and treatment will decrease the incidence of disfiguring surgery and increase cancer survival rates.
- It is necessary to write an accurate and complete description of abnormal clinical or radiographic findings in the patient's dental record so the proper follow-up can be accomplished.
- An exciting aspect of oral pathology is first creating a differential diagnosis and then determining a definitive diagnosis based on the elimination of improbable elements of the differential diagnosis.
- A definitive diagnosis should always be obtained for unknown oral or perioral abnormalities.

CHAPTER REVIEW

Case Study 1.1

Refer to Figure 1.55 for this case study. This panoramic radiograph was taken as part of an initial examination of a 25-year-old woman.

1. Write a radiographic description of the anomaly seen in the mandibular right posterior region. (Size is approximately 5 mm diameter.)
2. Based on the radiograph alone, what are some questions that you might want to ask this patient to determine a differential diagnosis?
3. How would you clinically evaluate the area?

For answers and additional review activities, log in to **thePoint.lww.com**

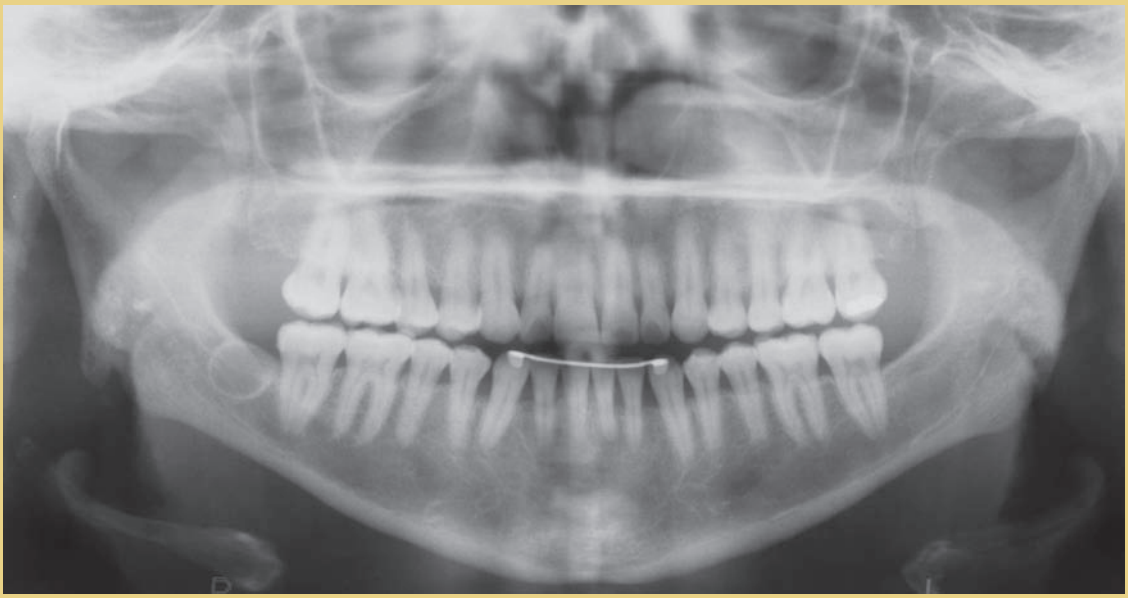

FIGURE 1.55.

Case Study 1.2

Your patient, Tracie, is a 34-year-old woman. Two days ago, you performed periodontal debridement with ultrasonic and hand instruments on her mandibular right quadrant. Tracie is returning for her second periodontal debridement today. Before beginning treatment, you review the medical and the dental history, obtain vital signs, and update her extra and intraoral examinations. You discover the lesion seen in Figure 1.56. You are quite startled at the bright red color and the fact the lesion was not there 2 days ago.

FIGURE 1.56.

1. Write a complete clinical description of the lesion (size approximately 1 cm in diameter, consistency soft).
2. Write out some questions you could ask her to help you determine a differential diagnosis.

   (Help: Look at the following conditions in Chapter 13—Petechiae, ecchymoses, and purpura; Erosive lichen planus; Erythematous candidiasis; Erythroplakia; Congenital hemangioma. Read about them and see if it helps to develop appropriate questions.)
3. Look at the conditions listed above and see if any can be eliminated based only on the information given in this case study so far.
4. In your opinion, what is the definitive diagnosis? Support your opinion with information from the case.

For answers and additional review activities, log in to **thePoint.lww.com**

Critical Thinking Activities

1. You have taken a position as a dental hygienist in an established practice. You are told what you are expected to accomplish during an initial appointment, maintenance appointments, and special appointments for sealants and periodontal debridement. You notice nothing has been said about a cancer screening examination. You ask if this is an oversight and are told that only the dentist performs the cancer screening examination. What are your initial thoughts about this? Do you think this is a good protocol for a dental practice? If yes, justify your answer. If no, what would you do to try to change it? Research your state's dental practice act and report on what the responsibility of the hygienist is in regards to this situation.
2. Refer to Figure 1.34 and the information in Application 1.2 for this activity. The patient has given you the following additional information: She states that she has experienced frequent dull aching sensations from the area that get sharper just before, during, and for a short time after she eats. Does the additional information bring you any closer to a definitive diagnosis of the lesion? If so, in what direction is it leading you?

Portfolio Possibilities

- Take photographs of pathologic or interesting atypical conditions you see in a clinical setting or copy several pictures of oral lesions from books and write complete clinical and/or radiographic descriptions of each one. Use your imagination to fill in the elements of consistency and size if necessary. Ask for your instructor's feedback on your project.
- Write a fact sheet for your patients about why the cancer screening examination (extraoral and intraoral examinations) is done and some examples of what you are looking for.

Media Menu

Web Sites

Healthy People 2020
http://healthypeople.gov/2020/default.aspx

Prevent Abuse and Neglect through Dental Awareness (P.A.N.D.A.)
http://www.healthy.arkansas.gov/programsServices/oralhealth/Pages/PANDA.aspx

Oral Health in America: A Report of the Surgeon General
http://www.nidcr.nih.gov/DataStatistics/SurgeonGeneral

dentalcare.com: Crest® Oral-B® online continuing education program The Intraoral and Extraoral Exam
http://www.dentalcare.com/en-US/dental-education/continuing-education/ce337/ce337.aspx?ModuleName=introduction&PartID=-1&SectionID=-1

Promoting the Patient Oral Self-Exam
http://www.dentalcare.com/en-US/dental-education/continuing-education/ce347/ce347.aspx?ModuleName=introduction&PartID=-1&SectionID=-1

Study Tools

Take advantage of additional online resources to help you study and ace your exams!

- Answers to case studies in the book
- Additional case studies and answers
- Interactive quiz bank with answer feedback
- Fully searchable e-book for quick lookup and studying on-the-go
- Expanded Media Menu with direct links to related Web sites and multimedia resources
- Supplemental references

thePoint Online resources and links are available at http://thepoint.lww.com/DeLong2e

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CHAPTER 2

Basic Pathology

KEY TERMS

Abscess
Apoptosis
Atrophy
Caseous necrosis
Coagulative necrosis
Complication
Dysplasia
Etiology
Exacerbate
Exocrine system
Free radical
Goiter
Hyperplasia
Hypertrophy
Hypoxia
Idiopathic
Incubation period
Integumentary system
Ischemia
Latent period
Liquefactive necrosis
Manifestation
Metaplasia
Morbidity
Mortality
Necrosis
Neoplasia
Pathogenesis
Pathology
Prognosis
Psychogenic
Relapse
Resistance
Resolution
Risk factor
Sequela
Sign
Stress
Susceptibility
Symptom
Xerostomia

LEARNING OUTCOMES

1. Define and use the key terms in this chapter.
2. List the different types of etiologies and give an example of each.
3. Determine whether an etiology is intrinsic or extrinsic.
4. List the major risk factors affecting the resistance of the host and state examples of each.
5. Describe how stress affects the body.
6. Describe elements that may be seen in the pathogenesis of a condition.
7. Explain the three major ways cells react to abnormal conditions.
8. Determine the type of cellular adaptation that has occurred, given certain characteristic features.
9. Differentiate between cellular adaptation, injury, and death.
10. List the most common mechanisms of cellular injury.
11. Identify instances in which apoptosis would most likely occur.
12. Describe the three different types of necroses.
13. Identify the type of necrosis associated with abscess formation.

CHAPTER OUTLINE

Concepts of the Pathologic Process
- Etiology
- Resistance and Susceptibility
  - Genetic
  - Immune System
  - First-Line Defense Systems
  - Age
  - Lifestyle
  - Stress
  - Environment
  - Preexisting Conditions
  - Multiple Risk Factors
  - Modifiable versus Nonmodifiable Risk Factors
- Pathogenesis
- Disease Manifestations
  - Cellular Adaptation
    - Atrophy
    - Hypertrophy
    - Hyperplasia
    - Metaplasia
    - Dysplasia
    - Neoplasia
    - Intracellular Retention of Substances
  - Reversible Cell Injury
    - Free Radical Injury
    - Hypoxic Cell Injury
    - Imbalance of Intercellular Calcium
  - Irreversible Cell Injury

RELATED CLINICAL PROTOCOLS

#10 Patient Education: UVA/UVB Skin Protection
#18 Supplements for Oral/Systemic Health
#24 Tobacco Cessation
#27 Motivational Interviewing for Behavior Change

Concepts of the Pathologic Process

Pathology is the study of disease or, more specifically, the study of abnormal conditions resulting from one or more of the following: disease, traumatic injury, structural or biochemical errors, genetic abnormalities, and so on. To study the disease process, the student must be aware of several factors. These factors include:

- The cause or **etiology** of the disease or pathologic entity.
- The events or characteristics that make certain individuals more susceptible or resistant to disease.
- The manner in which the disease progresses, or **pathogenesis.**
- The possible manifestations of disease on a cellular, tissue, and organ level.

This discussion not only involves disease as we know it but also describes other types of pathology, such as cuts, burns, acne infections, and arthritis.

Etiology

The first element in the development of disease or pathology is the causative factor, or the etiology. There can be a single cause, as in tuberculosis, or a multifactorial etiology, as in hypertension or heart disease. The first step in disease research is directed toward finding the etiology. Prior to knowing what the cause is, only the signs and symptoms of the disease can be treated. For example, as soon as acquired immunodeficiency syndrome (AIDS) was recognized, researchers began looking for the cause. Until it was found, physicians could only treat the opportunistic infections or conditions associated with the syndrome. As soon as the cause was determined to be viral and the virus was identified, finding a "cure" became possible. Current therapies for AIDS stress slowing down the replication of the virus, specifically inhibiting the ability of the virus to create proteins essential for its replication. The cause of most disease can be classified as either extrinsic (of external origin), intrinsic (of internal origin), or a combination of both. Table 2.1

TABLE 2.1 Extrinsic and Intrinsic Causes and Examples

Category	Etiology	Examples
Extrinsic	Pathologic organisms	Bacteria, virus, protozoa, fungus
	Physical agents	Temperature, electricity, ionizing radiation, UV radiation
	Chemical agents	Poison, acid, venom, drugs, lead, mercury
	Mechanical injury	Gunshot wound, motor vehicle accident
	Nutritional	Deficiency—scurvy, rickets
		Excess—obesity
	Iatrogenic	Infective endocarditis, hospital staphylococcus infection
Intrinsic	Genetic	Sickle cell disease, cystic fibrosis, some types of breast cancer
	Immunologic	Autoimmune—systemic lupus erythematosus
		Hypersensitivity—allergies
		Immunodeficiency—acquired immunodeficiency syndrome
	Degenerative	Osteoporosis, osteoarthritis

APPLICATION **2.1**

Pathology, by Any Other Name?

What is pathology, what is disease, and what is not? Many students are confused with terms such as abnormal, disease, lesion, condition and pathology. Consider, for example, an elderly woman with enlarged knuckles and pain when she first uses her hands in the morning. It is obvious she has some sort of arthritis, but is it pathology? Another example, a patient complains of a sore and swollen palate. The patient does not remember doing anything to cause the soreness. The hygienist examines the palate and finds a small torus palatinus with an abraded, red surface that looks very sore. Is this pathology? A teenager with a serious acne infection has a treatable condition, but is it a disease?

The first example is a disease and pathology. Osteoarthritis is a degenerative disease that can affect the entire skeletal system or just one area such as the hands. There are two conditions in the second example. The torus palatinus is considered a variation of normal with hereditary tendencies; as such, it is not considered a disease or pathology. On the other hand, the traumatic injury to the mucosal surface is considered a pathologic lesion, but it would not be considered a disease. In the third example, teenage acne is the result of many factors but is basically a bacterial infection of the skin; it is pathology but most would not consider it a disease and many think it is a "normal" condition because it is so common.

provides a list of intrinsic and extrinsic causes and examples. In addition to those causes listed in Table 2.1, pathology may be associated with psychogenic and/or idiopathic etiologies.

A disease state brought on by conscious or subconscious reactions or attitudes is considered to be **psychogenic.** The physical manifestations of psychogenic illness are often real and can prove incapacitating or fatal. No discussion of etiologies would be complete without the inclusion of the **idiopathic** etiology. When disease or pathology is determined to be of idiopathic origin, the causative agent or event has not been discovered. In many instances, it is not possible to name one etiologic agent or event as the cause of a particular pathologic process. Often there are several factors working together to produce disease in an individual. When there is more than one causative factor, the condition is said to have a multifactorial etiology. Multifactorial etiologies usually have a combination of extrinsic and intrinsic features. Heredity plays an important part in most of these conditions.

Resistance and Susceptibility

Why does one person develop an illness when others do not, even when they are exposed to the same conditions? The answer to this question lies within the realm of host resistance and susceptibility. **Resistance** is the natural ability of an organism to remain unaffected by pathogenic or toxic agents. **Susceptibility** is the exact opposite, where conditions within or around the organism or host do not inhibit the action of pathogenic agents. Resistance is affected by many **risk factors** or predisposing conditions. The following discussion focuses on general categories of risk factors (Box 2.1).

Genetic

Genetic influences play an undeniable role in whether or not a person is susceptible to certain conditions and diseases. In fact, it can be safely said that inheritance affects every aspect of our health. Some individuals have a limited genetic lineage, meaning that their ancestors may have the same ethnic or religious background or come from the same geographic area. Often, individuals in these groups have a higher risk of developing a disease than someone from another group. Families not having a limited genetic lineage may still carry genetic risk factors that will place them at a higher risk of developing conditions than families that do not have the risk factor. Tay-Sachs disease is a fatal genetic disorder affecting individuals of Jewish descent more frequently than any other group. Tay-Sachs disease is characterized by excess storage of lipids in the cells and tissues of the brain. This process eventually causes destruction of the cells and death of the child, usually within a few years. Sickle cell anemia is found most often in those with an African genetic lineage. Sickle cell anemia is the most common fatal genetic disorder among Blacks and is discussed in detail in Chapter 9. Often, inherited traits will decrease the resistance of an individual for certain conditions. Fair-skinned individuals have a higher risk of skin cancer than darker-skinned individuals. Higher risks of developing conditions such as breast cancer, heart disease, and high blood pressure have also been found in family lineages.

Immune System

A deficit in any part of the immune system will cause a decrease in the resistance of the host. Some defects are more serious than others. Loss of the tonsils for example, causes a minor decrease in the body's ability to fight off

BOX **2.1** **Major Groups of Risk Factors**

1. Genetic
2. Immune system dysfunction
3. Compromised first line defenses
4. Age
5. Lifestyle
6. Stress
7. Environment
8. Preexisting conditions

infection. In contrast, being born without the ability to manufacture properly functioning white blood cells causes severe **morbidity,** or disease, and most likely an early death from infection.

First-Line Defense Systems

First-line defense systems include the integumentary system and the exocrine system. The specific actions of this system are discussed in Chapter 3. The **integumentary system** includes the skin, hair, nails, and sweat and sebaceous glands. Damage to the skin can cause severe problems and even death. Burns on over 20% of the total body surface area are considered major burn injuries and result in massive fluid losses, electrolyte imbalances, and a decrease in blood volume, leading to shock and hypotension. In this case, the body is unable to maintain homeostasis because there is no external barrier protection in the area of the burns. The **exocrine system** comprises glands that excrete their products through ducts onto the surface of the skin or other organ. The exocrine system includes sweat glands, sebaceous glands, salivary glands, and glands of the gastrointestinal and respiratory systems. The antibodies found in these secretions help destroy invading organisms before they cause damage. The high pH of gastrointestinal secretions destroys many of the contaminants we ingest. Damage to any of the major salivary glands can result in **xerostomia** (inadequate salivary flow). Xerostomia and resulting oral complications are discussed in detail in Chapter 17.

Age

The body is less able to adapt to physical, biologic, and mental stresses at the beginning of life and in the later years of life. The older adult's defenses decline with advancing age and the infant's defense systems are not yet fully developed. Neither individual is able to mount an optimum response to infection or other stressors, resulting in the development of disease or pathology. Biologic and behavioral variations during different phases of life put an individual at risk for developing conditions at specific times during the life cycle. Osteoporosis is found more often in postmenopausal women because of decreased levels of the hormone estrogen (see Chapter 10). Middle ear infections are found more often in small children because of the structure of their ear. Car accidents were the leading cause of death for 13- to 19-year-old males and females in 2009, based on data from the U.S. Department of Transportation's Fatality Analysis Reporting System (FARS). Teenagers accounted for 11% of the U.S. population in 2010 and 10% of motor vehicle deaths (IIHS-HLDI, 2010).

Lifestyle

Lifestyle choices have a direct effect on resistance to disease. For example, smoking decreases the effectiveness of the immune system, leaving the smoker at higher risk for many lesser known problems, such as periodontal disease, in addition to the well-known consequences of heart and lung diseases. Dietary choices may increase the risk of cardiovascular disease and cancer. Frequent exposure to ultraviolet light, whether by choice or because of occupation, increases the risk of skin cancer. The problems associated with alcohol and/or recreational drug abuse affect all segments of society in the United States. Risky sexual behaviors can result in contact with the human immunodeficiency virus, syphilis, and/or gonorrhea, among others. Consequences of inappropriate lifestyle choices and behaviors are mirrored in the health of the body and the mind.

Stress

Stress can be defined as anything, physical or psychologic, causing the body to initiate the stress response, also known as the "fight-or-flight response." Many body functions are altered during this response. Box 2.2 lists physiologic changes that occur during the stress response. The stress response is intended to be a short-term action. For example, when individuals are startled, their hearts will beat faster to circulate more blood, they start breathing faster to increase oxygen in the body, they become very alert to their surroundings, and so on. When they realize nothing is wrong, everything returns to normal. This type of stress reaction is beneficial. Stress becomes harmful when the reaction is long term. Chronic stress produces the full range of actions summarized in Box 2.2, but to a lesser degree, over a longer time period. Eventually the body exhausts itself trying to keep up this heightened level of activity, exposing the individual to a higher risk for many conditions, such as cardiovascular disease, musculoskeletal disorders, psychologic disorders, and gastrointestinal disorders, among others.

Environment

The environment can be a risk factor for developing a disease or condition. For example, individuals living in the tropics have a higher risk of developing parasitic infections than those residing in colder climates. Family members living with a smoker have a higher risk of developing smoking-associated illness than those in a nonsmoking environment (American Lung Association, 2011).

Environmental exposure to toxic substances is a major concern. In the 1960s and 1970s, families living in Love Canal, a neighborhood in Niagara Falls, New York, were exposed to a myriad of toxic substances buried under the

BOX 2.2 Physiologic Responses to Stress

1. Increased blood flow to the heart
2. Increased blood pressure
3. Decreased blood flow to the extremities and to the stomach
4. Airways dilate to increase oxygen supply to blood
5. Increased amount of glucose available for energy
6. Increased mental alertness
7. Decreased unnecessary body functions such as digestion
8. Inhibition of some immune system cell functions
9. Increased fat generation and retention in the cells of the face and trunk

ground on which their homes and an elementary school were built. During the early and late 1970s, residents reported smelling strange odors and observing substances surfacing in their yards and seeping into their basements. The neighborhood had a very high rate of cancer and an alarming number of birth defects. Children who attended the school were always ill. This was the first case concerning hazardous waste disposal and possible health effects that received national attention in the media and at the highest level of government. The residents were relocated, some after years of legal battles. Most of the Love Canal site was eventually decontaminated, and a new community called Black Creek Village now stands on the land, but there is still an area that will not be habitable in any of our lifetimes (Love Canal Collection, 2006).

Preexisting Conditions

When an individual is compromised by one disease or condition, there is a much higher risk of developing a second disease or condition. Lesions of psoriasis, if scratched open, can become infected by bacteria. Conditions such as diabetes mellitus and cancer, and treatments for cancer, increase an individual's risk for contracting bacterial or viral infections. An individual with emphysema is more likely to develop pneumonia than someone who does not have a chronic lung condition.

Multiple Risk Factors

Risk factors may be found alone or in combination with others. The more risk factors involved, the higher the potential for disease development. For example, tobacco use increases oral cancer risk, but if alcohol use is added, the risk increases dramatically. Likewise, an individual with diabetes who also smokes has a high risk of developing periodontal disease, much higher than those with either risk factor alone.

Modifiable versus Nonmodifiable Risk Factors

All risk factors can be classified as either modifiable or nonmodifiable. Race, age, sex, and genetic background are nonmodifiable or unchangeable factors. Other risk factors may be modifiable by some individuals while nonmodifiable for others. For example, the 65-year-old executive may be able to retire from his or her stressful career, eliminating most of his or her life stress, while the 30-year-old single mother or father of three young children may not have that option. Many of our lifestyle choices are examples of modifiable risk factors including tobacco use, poor eating habits, risky driving behaviors, inappropriate drug use or abuse, and exercise habits, among others. In ideal situations, one would want to eliminate as many modifiable risk factors as possible to decrease the total risk of developing a condition. For example, knowing race, sex, and age are all nonmodifiable risk factors for developing hypertension or high blood pressure; a young Black man with a family history (genetic) of hypertension would want to maintain a healthy weight, exercise, monitor his sodium intake, not smoke, etc. to try to compensate for the risk factors he cannot change. Refer to Clinical Protocols 10, 18, 24, and 27.

APPLICATION **2.2**

Motivational Interviewing

One task that faces dental professionals is talking with patients about modifiable risk factors and facilitating discussions about behavior change. For example, if patients want to change their weight to decrease their risk of diabetes, they may contemplate changing their eating habits, starting an exercise program, or both. If patients want to decrease their risk of cancer, they may investigate ways to stop smoking.

Dental professionals should be comfortable discussing dental health issues, such as caries prevention with patients. Motivational interviewing (MI) is a patient-centered method that uses selective responses to patients' statements that assist in the resolution of ambivalence and moves the person toward change.

MI is a method of communication, not just a set of techniques, that focuses on eliciting the person's own reasons for change. It is not something that is done to a patient but rather a fundamental way of being with the patient; an interview in which the patient and professional are equal partners, neither of whom has more power or is more important. This method includes high-quality listening, but it also requires the specific use of methods to decrease resistance, resolve ambivalence, develop discrepancy, and trigger behavior change.

The main difference between behavior change counseling and MI is the dental professional's conscious and planned use of responses to elicit and reinforce certain kinds of speech, while reducing other types of patient responses. MI requires the dental professional to have the ability to be flexible, to tolerate uncertainty, to allow silence that allows thoughtfulness but not unnecessary anxiety, and the ability to refrain from providing solutions or arguments for change.

From Miller and Rollick. Motivational Interviewing—Preparing People for Change.

Protocol 27 presents a brief overview of Motivational Interviewing techniques. Additional online sources are listed at the end of this chapter in the Media Menu and on thePoint.

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Pathogenesis

Every disease or abnormality has a specific process of development or pathogenesis. Pathogenesis refers to the sequence of events during which cells or tissues respond to an etiologic agent. One may find individual variations under certain circumstances, but on the whole, the pathogenesis of a particular disease is usually the same from individual to individual. The pathogenesis of a disease may be very specific for a disease or it may be similar to other diseases or conditions. For example, the pathogenesis of syphilis is unique to this disease. No other disease mimics the primary, secondary, and tertiary stages of the disease process. Any stage taken alone can be mistaken for another process, but when viewed as a whole, there is no other similar condition. Chapter 12 provides more information on syphilis. The pathogeneses of measles (rubeola) and German measles (rubella) (see Chapter 11) are very similar to each other. Both diseases are viral, are transmitted through respiratory secretions, and infect the respiratory epithelium. Both cause cold-like symptoms with the addition of fever and a disseminated red rash. However, rubeola tends to be more serious and can be fatal in the young, elderly, or immunocompromised. Rubella, on the other hand, is less severe but has the distinction of being able to cause devastating birth defects, including spontaneous abortion or miscarriage. Laboratory tests and the clinical appearance of the rashes differentiate between the two; however, they are very similar.

A general understanding of some specific terms is helpful when discussing the pathogenesis of disease.

- The **incubation period** of a disease refers to the time in which the disease is developing but there are no overt signs or symptoms.
- A **sign** is an objective observation usually made by a clinician and sometimes a patient about the clinical manifestations of the disease process. Examples of signs include fever, rash, low blood pressure, and low red blood cell count.
- A **symptom** is a more subjective report of what a patient is feeling, such as fatigue, headache, and nausea, among others. In conversation, sign and symptom are often used interchangeably; however, an awareness of the difference is important in professional discussions.
- A **manifestation** is an observable or quantifiable characteristic associated with a specific type of pathology. Manifestations include signs, symptoms, results of laboratory tests, radiographs, and so on.
- The **latent period** is a time during disease development when there are no overt manifestations of the disease, although the disease can be found by using other means such as laboratory tests or radiographs. Herpes simplex (see Chapter 11) is an excellent example of a disease with latent periods. Following the primary infection, the virus lies dormant in the sensory ganglia of the trigeminal nerve in the head and neck area until an event activates it again. At this point, the virus manifests as a vesicular lesion, usually near the lips.
- **Exacerbation** refers to the worsening of a disease condition. For example, eating hot and spicy foods will exacerbate the pain of an oral ulcer.
- **Resolution** occurs when the affected individual or part returns to normal.
- The **sequela** of a disease is one or more conditions or pathologies that occur as a result of that disease. Male sterility is sometimes a sequela of mumps or acute viral sialadenitis (see Chapter 17).
- **Morbidity** refers to illness or disability associated with a disease. Morbidity is used more often in statistical discussions about the impact of a disease on a population.
- **Mortality** or death can also occur as a consequence of a disease process.
- A **complication** of a disease is an additional disease process or condition occurring at the same time and resulting from the conditions associated with the first disease process. For example, a bacterial sinus infection can be a complication of a cold. The bacterial infection would not have occurred if the viral cold had not produced the necessary environment of copious secretions and injured mucosal cells.
- A **relapse**, or flare-up, of a disease occurs weeks or months after the pathology was thought to be gone.
- The **prognosis** is an estimate of the most likely outcome of a disease, such as the likelihood the individual will survive or the pathology will resolve. The prognosis is based on many factors. For example, the pathogenesis of the disease, the condition of the individual, and the medical therapies available will all influence the prognosis.

Disease manifestations usually begin to be apparent as a disease or condition develops.

Disease Manifestations

Disease occurs in many forms, both visible and invisible. No matter what the cause or manifestation of a disease, it all begins on a cellular basis. The extent of a disease is related to how many cells are affected, and the seriousness may be related to which cells are affected. Because every disease is a manifestation of some sort of cellular change, disease should be studied by looking at what occurs on a cellular level. Cells react to abnormal conditions by adapting to the change (cellular adaptation), becoming injured (reversible injury), or dying (irreversible injury).

Cellular Adaptation

Changes inside the cell or in the area surrounding the cell occur as a result of normal or pathologic processes. Normal changes have as much of an effect on individual cells as pathologic changes. For example, the changes associated with pregnancy and the inevitable changes associated with aging are normal changes. Another normal process is the manner in which the body adapts to life at high altitudes. Less oxygen is available at high altitudes, causing the body

to compensate by producing more red blood cells to carry more oxygen to the tissues (secondary polycythemia, or erythrocytosis; see Chapter 9). Since this process takes time, travelers to areas of higher altitude experience shortness of breath much more quickly than normal for several days. This process, erythrocytosis, is also a manifestation of chronic obstructive lung disease (see Chapter 10). In this case, oxygen deprivation is caused by damaged lung tissues that impair the transfer of oxygen within the lungs. Pathologic changes are associated with infection, immune system dysfunction, traumatic injury, and many other factors. The adaptive process will continue until the stimulus for the change is removed and the environment returns to normal. If this does not happen, the cell may reach a point where it can no longer adapt to continued change, and internal damage will occur. In many cases, this damage is reversible if normal conditions are reestablished. If the damage continues, cell death or irreversible injury occurs.

Adaptive cellular changes include atrophy, hypertrophy, hyperplasia, metaplasia, dysplasia, and the intracellular retention of substances injurious to the cell (Fig. 2.1).

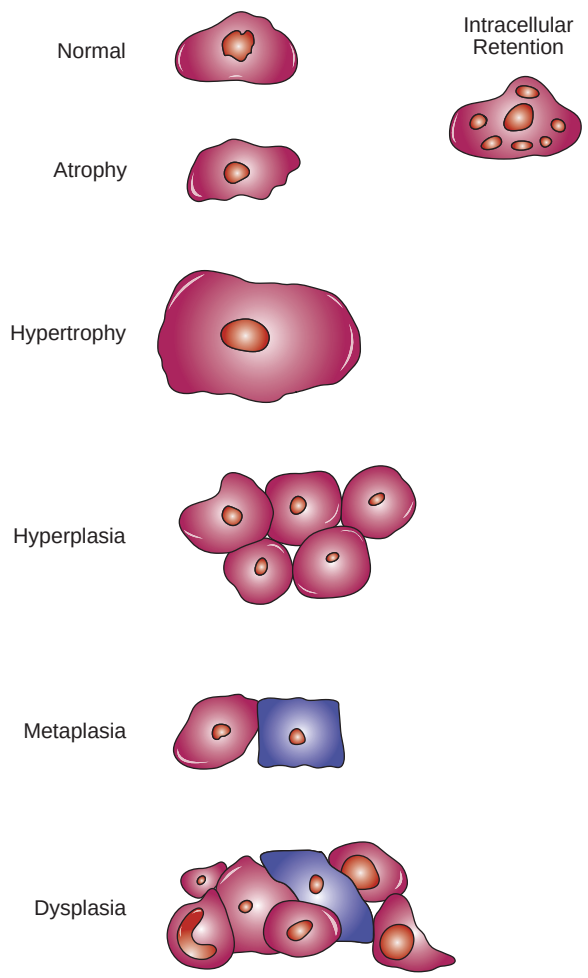

FIGURE 2.1. Cellular adaptation. Illustration comparing the different ways a cell can adapt to changes in its environment.

Neoplasia is a continuum of the process of dysplasia, but since neoplastic growth is not considered an adaptive change, it is only mentioned here and is discussed in depth in Chapter 5.

Atrophy. **Atrophy** is a decrease in the size and function of a cell, tissue, or organ, caused by one or more of the following conditions: reduced functional demand, hormonal stimulation, nutrient supply (including oxygen), and/or the normal process of aging. Reduced functional demand on a cell, tissue, or organ will cause it to decrease in size. For example, when a cast is removed from a broken arm or leg, there is an obvious difference in size between the previously broken limb and the limb that was not broken. This occurs simply because the limb was not allowed to function for a length of time. The same condition occurs with paralyzed body parts, because there is no longer any neural stimulation of the affected area. Musculoskeletal disorders such as carpal tunnel syndrome cause atrophy of the affected areas (Fig. 2.2).

Atrophy also occurs in response to a reduction in hormonal stimulation. The ovaries atrophy after menopause because they no longer receive hormonal stimulation from the pituitary gland. Reduced nutrient supply may also cause atrophy. Muscle and organ atrophy is associated with anorexia nervosa and with many cancers. In anorexia nervosa, the cells are not receiving nutrients because they are not getting them from the individual; in cancer, the individual's nutrients are being devoured by the out-of-control demands of the cancerous growth. Atrophy caused by a reduction of nutrients may occur in areas of chronic cellular injury, such as areas involved with a persistent bacterial infection.

A decreased supply of oxygen, or **ischemia,** will cause cell atrophy. This type of atrophy is usually seen in areas where vascular damage has occurred, such as the damage done during a myocardial infarction or heart attack (see Chapter 8). Cellular atrophy occurs in the normal process of aging. The best examples of this are seen in the aging heart muscle and brain.

Hypertrophy. **Hypertrophy** is the enlargement of individual cells leading to an increase in the size of the tissue

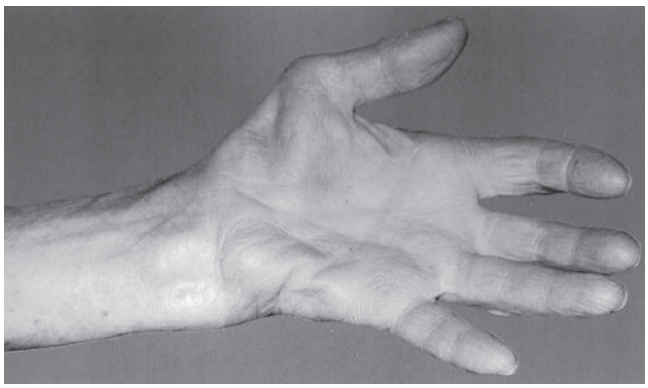

FIGURE 2.2. Atrophy. Atrophy of the thenar muscles at the base of the thumb due to chronic compression of the median nerve (carpal tunnel syndrome). (From Moore KL, Dalley AF. Clinical oriented anatomy. 4th ed. Baltimore: Lippincott Williams & Wilkins, 1999.)

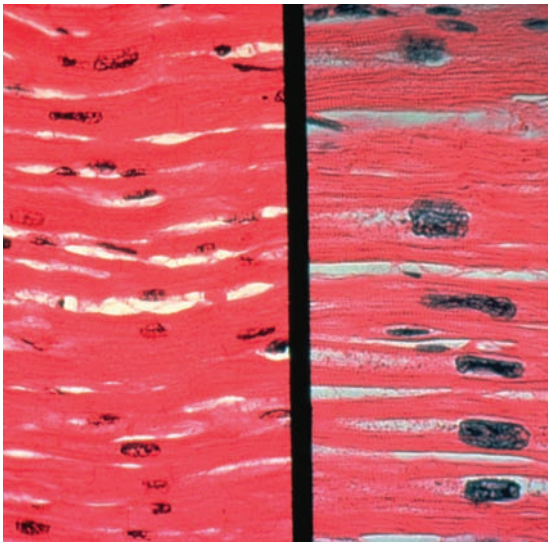

FIGURE 2.3. Hypertrophy. Myocardial hypertrophy. Compared with a normal myocardium (**left**), the hypertrophic myocardium (**right**) shows thicker fibers and enlarged, hyperchromatic, rectangular nuclei. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

or organ and is commonly caused by increased functional demand or hormonal stimulation. The increase in size may also result in an increase in the functional capacity of the tissue or organ.

Hypertrophy caused by an increase in the functional demand placed on the cells is best exemplified by the increase in muscle mass due to weight lifting or exercise. Muscle cells do not replicate; therefore, the increased demand of strenuous exercise will stimulate hypertrophy. Hypertension (see Chapter 8) causes an increased demand on the heart muscle, which in turn causes individual cells to become hypertrophic (Fig. 2.3). The end result in this case is hypertrophy of the left ventricle, which is being overworked to pump blood through peripheral arteries that have lost their elasticity (Fig. 2.4).

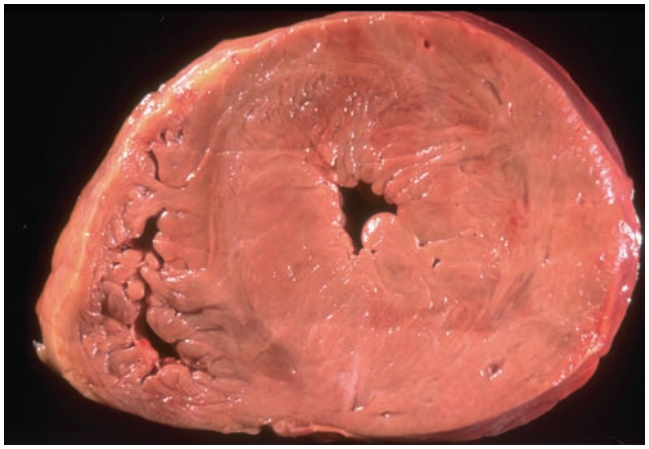

FIGURE 2.4. Ventricular hypertrophy. Cross section of the heart of a patient with long-standing hypertension shows pronounced, left ventricular hypertrophy. (From Rubin E, Farber JL. Pathology, 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

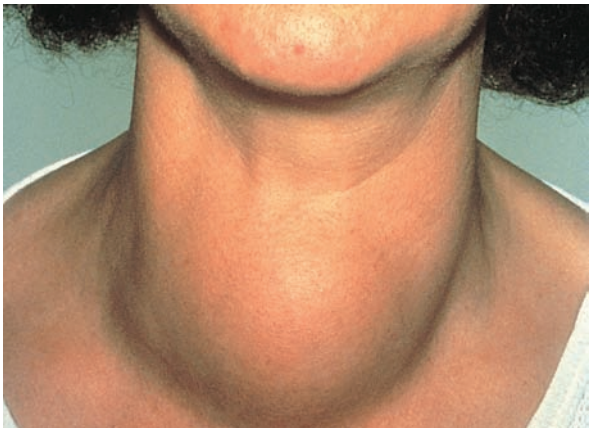

FIGURE 2.5. Hypertrophy and hyperplasia. Diffuse enlargement of the thyroid gland, called a goiter, usually results from a combination of hypertrophy and hyperplasia. (From Weber J, Kelley J. Health assessment in nursing. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

Hypertrophy caused by excessive hormonal stimulation occurs in the thyroid gland (see Chapter 7) when there is an inadequate dietary intake of iodine. The pituitary gland reacts to the low level of circulating thyroid hormones by sending out more thyroid-stimulating hormone (TSH), to the thyroid gland. This overstimulation will induce the cells of the gland to enlarge to produce more thyroxine, creating a **goiter** (Fig. 2.5).

Hyperplasia. **Hyperplasia** is an increase in the number of cells in a tissue or organ, resulting in enlargement. Hyperplasia may be the result of excessive hormone stimulation, chronic cell injury, increased functional demand, or extensive cell injury or death. Hormonal stimulation of the uterine lining during pregnancy causes hyperplasia of these cells. The creation of more red blood cells in those living at high altitudes, called secondary polycythemia, is an example of hyperplasia caused by increased secretion of the hormone erythropoietin by the kidneys. This hormone is released in response to a decreased level of oxygen in the blood. Constant irritation of epithelial cells in the skin causes a callous or epithelial hyperplasia at the point of friction. Figure 2.6 shows an area of hyperplasia within the epidermis that could have occurred in response to chronic irritation. Liver cells will become hyperplastic to replace cells lost because part of the liver is removed.

Hyperplasia often occurs in conjunction with hypertrophy in tissues able to replicate. For instance, in the goiter example, hypertrophy and hyperplasia usually occur concurrently because the glandular tissue is able to replicate (see Fig. 2.5). Cardiac muscle, on the other hand, will only hypertrophy, because it is not able to replicate.

Metaplasia. **Metaplasia** is the conversion of one differentiated cell type to another. Chronic irritation or inflammation may initiate the transformation from the normal cell to one that may be better able to survive in the environment altered by the chronic condition. Some of the most common examples of this process occur in smokers. The

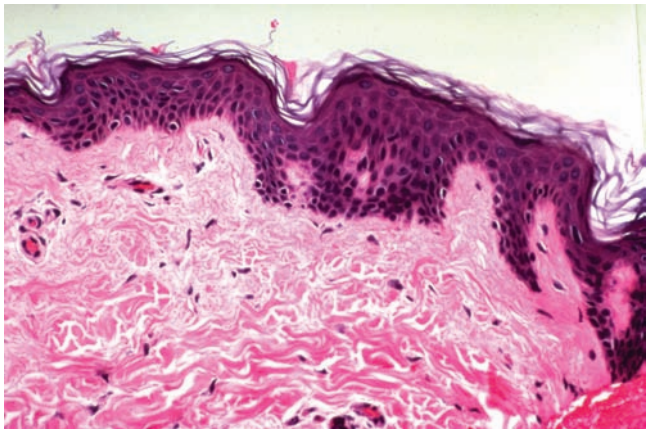

FIGURE 2.6. Hyperplasia. Normal epidermal tissue is seen on the left, hyperplastic tissue is seen on the right. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

bronchial epithelium undergoes a metaplastic change from normal cells that have cilia and produce mucus to squamous epithelium that functions as a protective barrier only. This might appear to be in the best interest of the host; however, the metaplastic change compromises the natural protective ability of the lungs to provide ciliary clearance and produce mucous. The olfactory epithelium is also at risk for metaplastic change as seen in Figure 2.7.

A metaplastic change may occur in cases of gastroesophageal reflux disease (see Chapter 10). The esophageal epithelium is changed to a type of gastric mucosa that has more protective ability than the normal esophageal lining epithelium. If the cause of the metaplasia is removed, the cells will eventually revert to the normal type. This is an adaptive process; however, dysplastic and even neoplastic changes have been observed in areas of metaplastic change.

Dysplasia. **Dysplasia** refers to the creation of abnormal cells from normal cells. The abnormalities include changes in the size and shape of the cell along with nuclear changes within the cell and the irregular arrangement of the cells within the tissue (Fig. 2.8). There is controversy surrounding dysplasia. Some say it is an adaptive process; others believe it is a neoplastic process. Most consider dysplasia to be a premalignant condition. Often malignant lesions will be surrounded by areas of dysplasia. Dysplasia is classified as mild, moderate, or severe. Severe dysplasia is so similar to cancer that in many cases it is assumed to be and treated as such. If the cells are truly dysplastic and the stimulus causing the dysplasia is removed, the cells will revert to their normal state. If the stimulus is removed and the cells continue to reproduce uncontrollably, then a true neoplastic process is taking place.

Neoplasia. **Neoplasia** is defined as a new growth of cells. Neoplastic growth is not an adaptive change but rather a pathologic growth of cells. Neoplastic cell growth is not regulated by the elements that normally control the growth

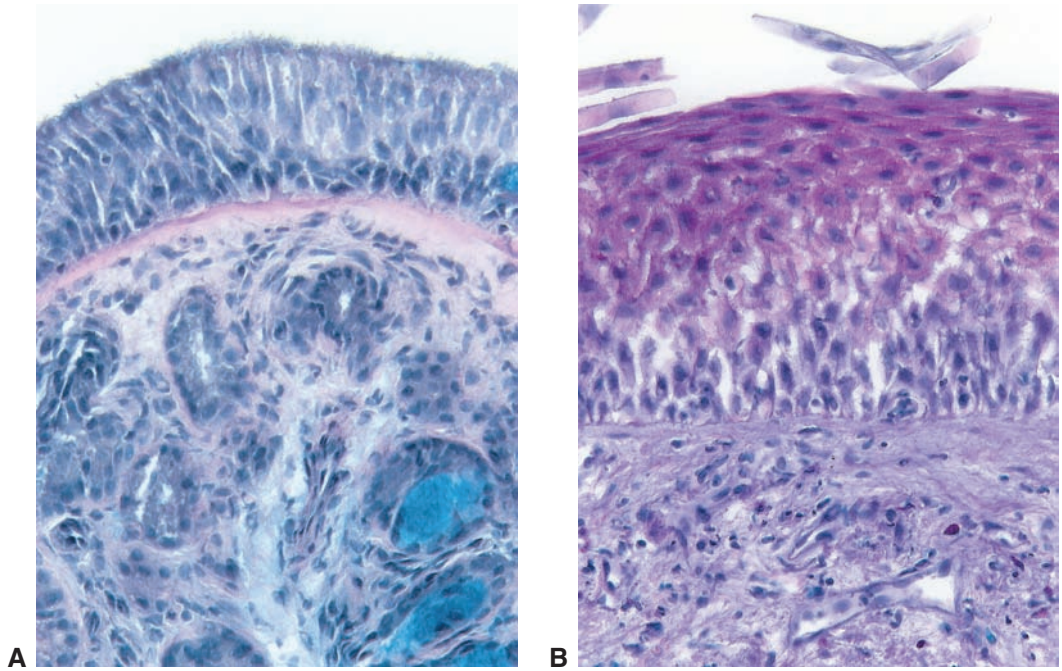

FIGURE 2.7. Metaplasia. The olfactory epithelium is susceptible to injury from many sources, such as environmental exposure to toxic substances (tobacco and other toxins), trauma, sinus diseases, inflammation, and aging. These factors often lead to epithelial changes. Pictured are sections of human nasal biopsies. **A.** *Normal*. Normal pseudostratified sensory epithelium contains a layer of basal cells at the base of the epithelium, multiple layers of immature and mature olfactory sensory neurons and a surface layer of microvillous olfactory cells. **B.** *Severe Metaplasia.* In severe squamous metaplasia, several layers of distinctive squamous-like cells and flattened squamous-like cells without microvilli are observed replacing the normal olfactory cells in the olfactory epithelium. (Images courtesy of Karen Yee with funding support from National Institute on Deafness and Other Communication Disorders DC006760.)

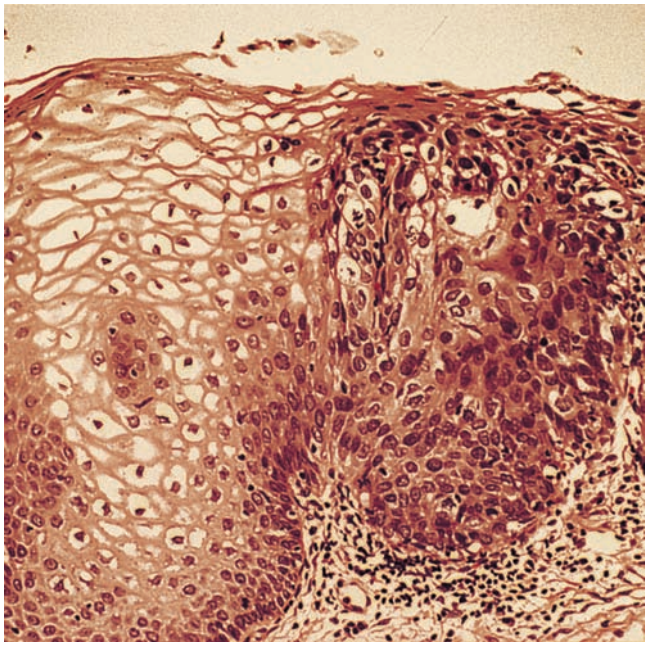

FIGURE 2.8. Dysplasia. A section of the cervix shows an area of epithelial dysplasia (**right**) adjacent to an area of normal squamous epithelium. The dysplastic epithelium lacks the normal layering of cells at different stages of maturation and the individual cells show hyperchromatic nuclei, a larger nucleus-to-cytoplasm ratio, and a disorderly arrangement. (Image from Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

of cells; thus, cell growth continues unchecked. Neoplastic growth is covered in depth in Chapter 5.

Intracellular Retention of Substances. In some cases, cells may retain or store certain substances that are either normally present in smaller quantities or are pathologic. This is also an adaptive process, and if the reason for the storage of these substances is removed, the cell will return to normal. Overingestion of foods rich in carotene such as carrots, squash, pumpkins, and others can result in carotenemia (Fig. 2.9). Carotenemia occurs when excess carotene is stored in the epithelial cells; it is not harmful and the color will dissipate when the dietary intake of these foods is decreased. Many genetic diseases cause errors in the creation or metabolism of important cellular substances. Hepatitis A infection will cause skin and mucous membranes to turn yellow or become jaundiced. This is due to an excess amount of bilirubin in the affected epithelial cells (Fig. 2.10). Bilirubin is stored in the epithelial cells because the infected liver is not functioning correctly. When the liver recovers and begins to work correctly, the color dissipates. Often these abnormal substances cannot be used by the cells or removed from them, and their accumulation becomes toxic to the cell. The substances accumulate in cells until the cell is no longer able to adapt to the accumulations, at which point the cell dies. Tay-Sachs disease is an uncommon genetic disease resulting from the accumulation of an abnormal glycoprotein in the cells of the brain and nervous system (Fig. 2.11). The glycoprotein is toxic to

FIGURE 2.9. Carotenemia. Note the yellow color of the hand on the left compared to the normal pink hand on the right. The yellow color is due to intracellular retention of carotene resulting from excess dietary consumption of highly pigmented fruits and vegetables, carrots in this case. (From Bickley LS and Szilagyi P. Bates' guide to physical examination and history taking. 8th ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

the cells and causes their death. Children with Tay-Sachs disease normally survive little more than 1 year.

Reversible Cell Injury

Reversible cellular injury occurs if there is persistent or chronic damage or if the cell is no longer able to adapt to changes in the ways discussed above. This section provides a brief introduction to the mechanisms by which reversible cellular damage occurs, to promote awareness of the current concepts in treatment for various pathologic conditions. Reversible cellular injury most commonly results from free radical injury, hypoxic injury, and/or impairment of calcium balance within the cell.

Free Radical Injury. A **free radical** is a highly reactive class of chemical that is generated by the cell during most of its normal metabolic processes. Oxygen is the most frequent source of free radicals because it has two unpaired outer

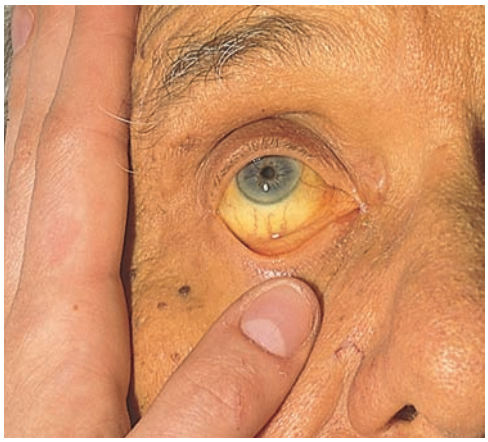

FIGURE 2.10. Intracellular retention of bilirubin. A yellow sclera and the yellow cast of the skin indicate jaundice. (From Bickley LS, Szilagyi P. Bates' guide to physical examination and history taking. 8th ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

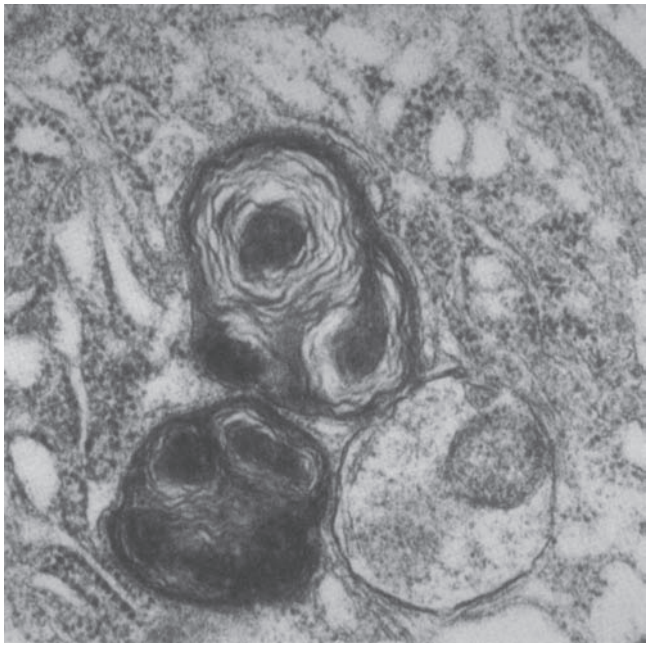

FIGURE 2.11. Abnormal retention of substances within the cell. Tay-Sachs disease. The cytoplasm of the nerve cell contains lysosomes filled with whorled membranes. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

electrons and is used in almost all of the cell's activities. Normally the cell has built-in defenses against free radical injury; however, when the cell is under stress for any reason, these defenses can become impaired. Impaired defenses against free radical injury allow single-strand breaks in DNA to occur. The phospholipids in the cell membrane and organelle membranes can be destroyed, compromising the integrity of these structures, which impairs the normal function and replicative capabilities of the cell. In addition, cell membrane disruption will upset the balance of calcium within the cell, which causes even more problems.

Hypoxic Cell Injury. In **hypoxic** cell injury, a lack of oxygen to the cells inhibits or stops the production of energy within the cell. Without energy, the cell is not able to survive. One of the first manifestations of oxygen deprivation, or ischemia, is an increase in the amount of water in the cell. This occurs because the cell depends on an energy source to actively maintain the sodium/potassium balance within it. If that mechanism is not working because there is no source of energy, then sodium and water will flow unchecked into the cell causing swelling (Fig. 2.12). The imbalance of minerals and water within the cell also allows intercellular substances, usually enzymes, to leak into the surrounding tissues and be picked up by the circulatory system. These substances are markers for cell injury and can be detected in laboratory tests that target their presence. This is an important factor in diagnosing many conditions that are characterized by cell injury and death. For example, the presence of certain cardiac enzymes in the blood can diagnose a myocardial infarction or heart attack because those enzymes would not be present unless cardiac cells had been destroyed. If hypoxia is severe enough or lasts for a long time, cell death can result. Oxygen deprivation can be partial or total. Partial deprivation occurs in anemia (see Chapter 9) or obstructive lung diseases such as emphysema or chronic obstructive bronchitis (see Chapter 10).

APPLICATION **2.3**

Blueberries, Avocados, and Red Wine

Free radical injury has been associated with many chronic diseases including atherosclerosis, cancer, Parkinson disease, and Alzheimer disease. The production of free radicals by the cell during metabolism has been compared to the production of ashes when a fire burns; both are the leftovers of oxidation. Our bodies can defend themselves against this injury most of the time by using antioxidants, which are produced by the cells. However, as we age, the abilities of this defense system diminish, manifesting more chronic diseases with aging. Consider the following question being researched today: If oxidation damages our bodies and antioxidants help to protect us from this damage, if we introduce more antioxidants into the equation (e.g., through dietary supplementation), will it help to stop or reverse the process? One method of increasing the amount of available antioxidants in the body is to increase the dietary intake of foods high in antioxidants. The most common antioxidants are vitamin C, vitamin E, and β-carotene. Some trace elements have also been recommended including selenium, copper, zinc, and manganese. To date, research has not been favorable for curing the degenerative neurologic diseases such as Alzheimer or Parkinson disease. The risk of some cancers, such as colon cancer and breast cancer, may be reduced when more fresh fruits and vegetables are introduced into the diet (see Internet Resources for sites listing antioxidant-rich foods). However, researchers have not concluded that it is the antioxidant properties of these foods that are beneficial. Increasing ingestion of antioxidant-rich foods may help decrease the formation of atherosclerotic plaques that lead to heart attacks and strokes. The American Heart Association has recommended establishing a balanced diet with an emphasis on antioxidant-rich fruits, vegetables, and whole grains to influence the risk of disease in the general population (Lichtenstein et al., 2006).

Many believe the key to preventing the effects of aging is somehow associated with antioxidants. One theory of aging proposes the process may be due to an accumulation of cellular injuries caused in part by free radicals. This raises the question: will antioxidant therapy be the key to the fountain of youth? Research involving the role of antioxidants in the prevention of human disease continues to be done, but as of 2011 there is still no consistent or conclusive evidence to support anything more than the American Heart Association's 2006 dietary recommendations (Obrenivich et al., 2010).

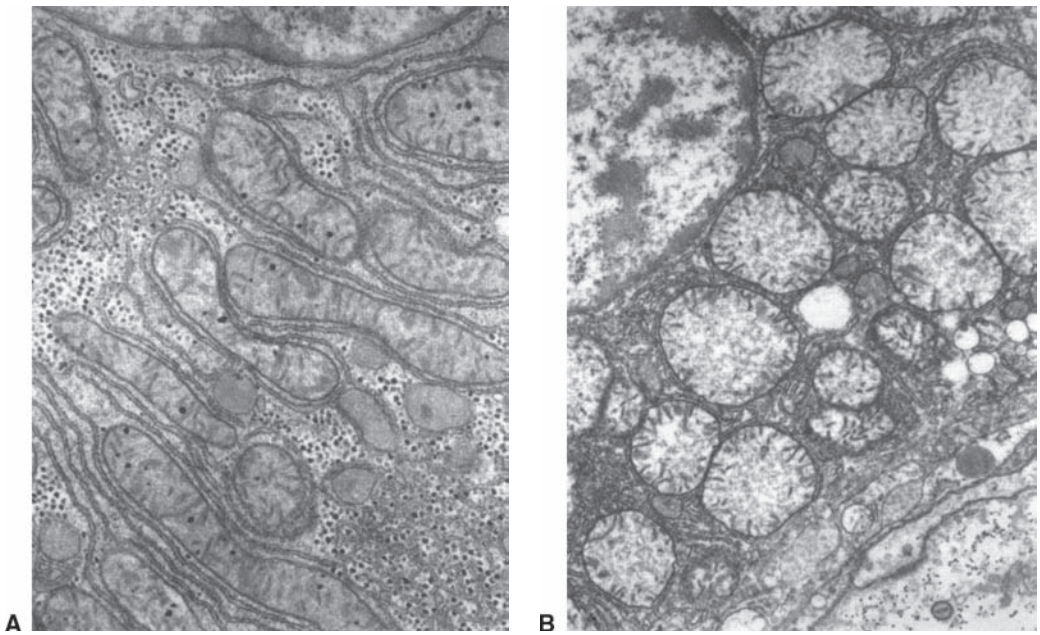

FIGURE 2.12. Hypoxic cell injury. Mitochondrial swelling in acute hypoxic cell injury. **A.** Normal mitochondria are elongated and display a dense mitochondrial matrix. **B.** Mitochondria from a hypoxic cell are swollen and round and exhibit a decreased matrix density. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

Total deprivation occurs when, for example, a blood vessel is completely obstructed during a stroke or a myocardial infarction (see Chapter 8). The type of cell determines how long the cell can go without any oxygen. Cells that are well differentiated, such as brain and heart cells, can withstand only minutes of complete oxygen deprivation without irreversible damage, while skin cells may survive for hours without oxygen. The ability of the cell to produce energy anaerobically or without oxygen is also important. Skeletal muscle cells can work longer under hypoxic conditions because they can produce energy without using oxygen for short periods of time. If the oxygen supply is reestablished soon enough, cellular damage may be reversible.

Imbalance of Intracellular Calcium. When the system maintaining the sodium and potassium levels in the cell fails, the system that maintains the calcium and magnesium levels will also fail. Normal cells have less calcium inside them than is found in the extracellular environment. When the mechanism that maintains this balance fails, there is an influx of calcium into the cell. Increased levels of calcium activate enzymes that can damage the cell and compromise the cell membrane, eventually causing lysis or death of the cell.

Irreversible Cell Injury

Two basic classifications of cell death include apoptosis and necrosis. **Apoptosis** is cellular self-destruction. It is common knowledge that many tissues of the body are constantly producing new cells; imagine if there was no way to get rid of the old cells. The result would be very large bodies. The average adult produces about 10 billion new cells every day and destroys about the same number. In the process of apoptosis, the cell nucleus disintegrates and the cell falls apart (Fig. 2.13). The remnants of the cell are digested by phagocytic cells and removed via the lymphatic system. Aging white blood cells are removed from the body through the process of apoptosis. If they were not removed, for instance, a pathologic accumulation of white blood cells, or leukemia, would occur. Epithelial cells that form the lining of the intestines undergo the process of apoptosis. Also, in fetal development, the formation of separate digits from webbed fingers is a result of apoptosis. Apoptosis is usually a normal process; however, it can also be triggered by stimuli such as viral infections or mutagenic agents.

Necrosis is another type of cell death. If the cell is unable to adapt to its environment by nonlethal means such as hypertrophy or if the changes are too deleterious to the cell over the long term, the cell will undergo necrosis. Caseous necrosis, coagulative necrosis, and liquefactive necrosis are among several types of necroses. **Caseous necrosis** is specific to the lesions found in the lungs of individuals with

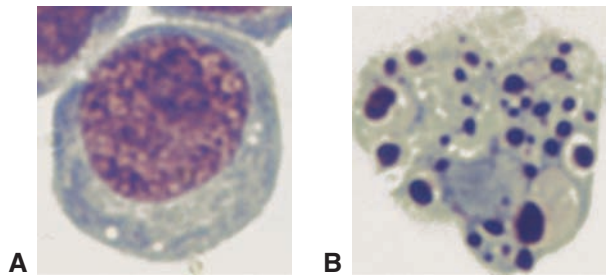

FIGURE 2.13. Apoptosis. A viable leukemic cell **(A)** contrasts with an apoptotic cell **(B)** in which the nucleus has undergone disintegration. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

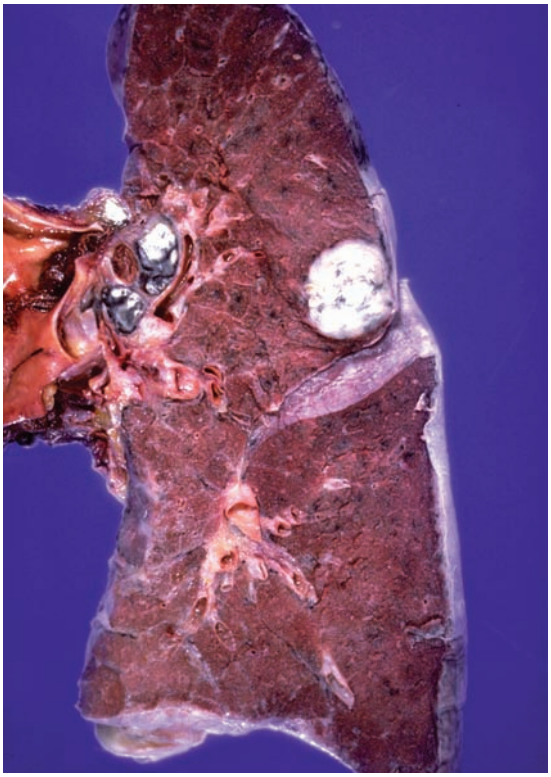

FIGURE 2.14. Caseous necrosis. The white cheesy substance is the caseous necrosis seen in tuberculosis. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

tuberculosis. The lesions are called tubercles (Fig. 2.14), and as the cells inside the tubercle become necrotic, they form a thick cheesy, or caseous, material. **Coagulative necrosis** occurs primarily when there has been cell hypoxia or ischemia, as in a myocardial infarction. When the cells die, they become firm and opaque. Figure 2.15 depicts the darker streak of necrotic cardiac cells that contain no nuclei

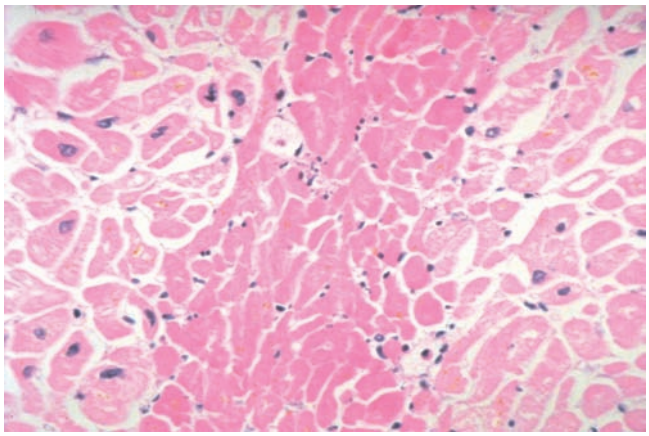

FIGURE 2.15. Coagulative necrosis. A photomicrograph of the heart in a patient with an acute myocardial infarction. **Center**, The deeply colored necrotic cells have lost their nuclei. The necrotic focus is surrounded by paler-staining, viable cardiac cells. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

FIGURE 2.16. Liquefactive necrosis. This periapical abscess associated with a mandibular molar is an example of liquefactive necrosis.

and are characteristic of coagulative necrosis. **Liquefactive necrosis** occurs when the body is dealing with a bacterial infection, especially by staphylococci and streptococci. White blood cells that rush to the area are armed with potent enzymes that destroy not only the bacterial invaders but also the cells of the host. This action takes place in an area that is walled off from the surrounding healthy tissue. The body is unable to remove the debris as fast as it is being produced, resulting in an **abscess,** which is an accumulation of dead cells, dead bacteria, and dead and dying white blood cells. Figure 2.16 shows an abscess in the right cheek caused by a dental or periapical abscess involving one of the mandibular right molars. Figure 2.17 shows a draining abscess resulting from a spider bite. Figure 2.18 provides a summary of the process of cellular injury.

The process of cell injury and death does not occur without a response from the body of the host. These responses include the inflammatory response, the immune response, and the process of healing and repair. These topics are discussed in depth in the following chapters.

FIGURE 2.17. Liquefactive necrosis. A spider bite resulted in this draining abscess. Note the area of necrosis in the center of the abscess.

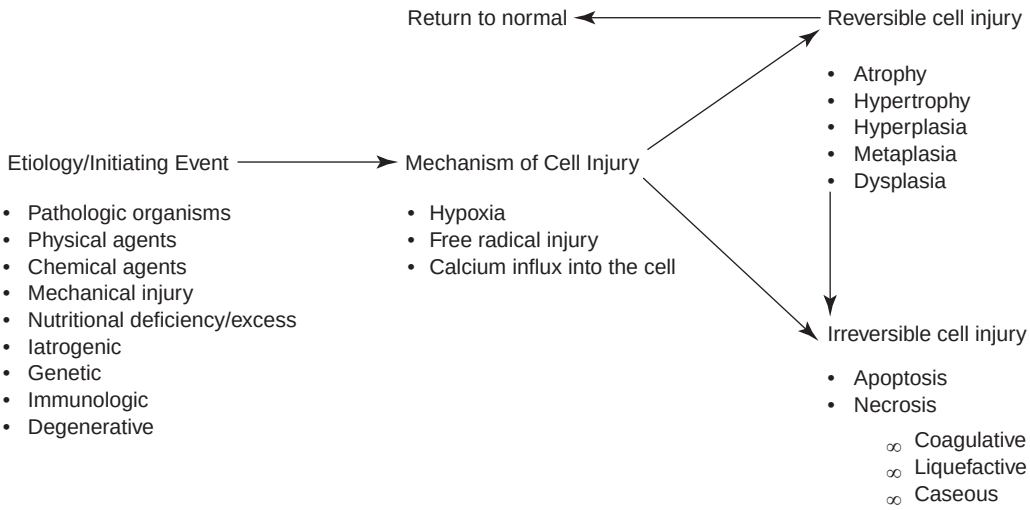

FIGURE 2.18. Summary of the process of cellular injury.

SUMMARY

- The first element in the study of disease is the etiology. There are intrinsic and extrinsic causes. Pathogenic organisms, physical agents, chemical agents, mechanical injury, and nutritional factors are extrinsic causes. Genetic, immunologic, and degenerative diseases are intrinsic causes.
- Whether or not an individual actually acquires a disease or condition depends on many variables or risk factors that determine resistance and susceptibility. The risk factors can be placed into major groups, including immune system dysfunction, compromised first-line defenses, age, inheritance, risky lifestyle behaviors and choices, undue stress, environmental exposures, and preexisting conditions.
- Age, sex, race and genetic makeup are nonmodifiable risk factors. Other risk factors such as weight, activity level, diet, and more are considered to be modifiable, and a decrease in these risk factors can decrease total risk for disease development.
- When an individual acquires a condition, the sequence of events in the development of the disease is called the pathogenesis.
- All disease manifestations are first evident on a cellular level. The clinical manifestations of the condition will depend on which cells and how many cells are affected.
- Cells can adapt, undergo reversible injury, or die. Cells adapt through atrophy, hypertrophy, hyperplasia, metaplasia, and dysplasia and by retaining certain intracellular substances.
- If reversible injury is not stopped, the cell will die. The normal process of cell death is called apoptosis. Pathologic cell death is necrosis.
- There are several types of necrosis; liquefactive necrosis may lead to the formation of an abscess. Other forms occur in response to ischemia and specific diseases.

CHAPTER REVIEW

Case Study 2.1

Refer to Figure 2.19.

1. Write a clinical description of what is seen in this image.
2. Is this an example of reversible or irreversible cellular damage? Justify your answer with elements from your description and note the specific type of reversible or irreversible damage you believe is exemplified in this image.

For answers and additional review activities, log in to **thePoint.lww.com**

FIGURE 2.19.

Case Study 2.2

A 40-year-old male who has been a patient in your office for several years has an appointment for dental hygiene care. You have never seen him for any procedures because he has always come for evening appointments. You review his medical history, take vital signs, and update his personal information. There are no significant findings. Findings from your extraoral examination are normal. As you perform your intraoral examination, you see the condition pictured in Figure 2.20. You question the patient about the appearance of his tongue.

1. What type of questions would you like to ask this patient?
2. How would you describe the lateral surface of the tongue?
3. What do you think has caused the condition?
4. What could be done to help resolve the condition and prevent it from recurring?
5. What type of cellular adaptation has most likely occurred within the tissues of the tongue?

FIGURE 2.20.

For answers and additional review activities, log in to **thePoint.lww.com**

Critical Thinking Activities

1. **A.** If we could somehow know our integumentary system was totally intact, would we need to wear gloves while performing clinical procedures?
   B. How can you be sure your skin is totally intact?
   C. How can you be sure your gloves are totally intact?
   D. What precautions do you take to try to make sure no contamination reaches your hands even though you are using gloves?
2. **A.** Construct a list of conditions you think might be associated in some way with the age of an individual.
   B. Explain why you have included each condition on the list and share your list with your classmates.
   C. Can you think of any reason such a list might be useful in your practice of dental hygiene?
3. **A.** Consider the lifestyle choices you have made. Categorize them by whether you think they are healthy, unhealthy, or neutral. Think of how you might eliminate or modify some of the unhealthy choices, then think of ways you can maintain the healthy choices.
   B. Do you think encouraging patients to examine their lifestyle choices is part of your "job description"? Why or why not?

Portfolio Possibility

- The role of the dental hygienist is expanding and we often find ourselves faced with a patient asking for advice about issues sometimes far removed from traditional "dental matters." Sometimes you will already know the answers to patients' questions or where they can go to get help. However, it will be an asset to have access to some of this information at your fingertips. Think of the various categories of risk factors and find resources (community, internet, other) you could refer someone to if he or she needed help or information in any of these areas, for example, tobacco cessation. Create a listing or booklet with the information so you can readily provide it to your patients when they ask instead of having to get back to them at a future time.

Media Menu

Web Sites

Motivational Interviewing—resources for clinicians, researchers, and trainers
http://motivationalinterview.net/

The American Geriatrics Society—information on aging
http://www.americangeriatrics.org/

Multimedia Resources

Apoptosis animation
http://youtu.be/xkASer3gEnc

The Effective Dentist: Motivational Interviewing Demonstration
http://youtu.be/f8QSA_5PEFM

Study Tools

Take advantage of additional online resources to help you study and ace your exams!

- Answers to case studies in the book
- Additional case studies and answers
- Interactive quiz bank with answer feedback
- Fully searchable e-book for quick lookup and studying on-the-go
- Expanded Media Menu with direct links to related Web sites and multimedia resources
- Supplemental references

thePoint Online resources and links are available at http://thepoint.lww.com/DeLong2e

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CHAPTER 3

Inflammation and Repair

KEY TERMS

Abscess	Leukocytosis
Acute inflammation	Leukotrienes
Adhesion	Lipopolysaccharide (LPS)
Agranulocytes	Ludwig angina
Alternative pathway	Lymphocytes
Alveolar osteitis	Lysosomal enzymes
Angiogenesis	Lysosome
Bacteremia	Macrophage
Basophils	Margination
Bradykinin	Mast cell
Cardinal signs of inflammation	Membrane attack complex
Cascade	Microcirculation
Cellulitis	Monocyte
Chemical mediator	Motile phagocytes
Chemokine	Opsonins
Chemotaxis	Opsonization
Cicatrix	Pavementing
Classic pathway	Permeable
Clotting system	Phagocyte
Complement system	Phagocytosis
Cytokines	Phagosome
Edema	Plasma cells
Emigration	Plasma fluid
Endothelium	Platelet-activating factor
Eosinophils	Polymorphonuclear neutrophils
Epithelialization	Prostaglandin
Fibroblasts	Pyogenic
Fibrous repair	Pyrexia
Fistula	Pyrogen
Giant cell	Regeneration
Granulation tissue	Repair
Granulocyte	Resolution
Granuloma	Septicemia
Granulomatous inflammation	Serotonin
Histamine	Serous exudate
Hyperemia	Transmigration
Immunoglobulins	Tumor necrosis factor (TNF)
Interleukin-1 (IL-1)	Vascular stasis
Keloid	Vasoconstriction
Kinin system	Vasodilation
Leukocyte	

LEARNING OUTCOMES

1. Define the terms used to describe the inflammatory process.
2. Describe the normal sequence of events in the acute inflammatory process.
3. Describe the function of each type of cell that takes part in the acute inflammatory process.
4. Identify and describe the functions of the major chemical mediators involved in the inflammatory process.
5. Identify the two major forms of exudate.
6. List the positive aspects of edema.
7. Identify the expected outcomes of acute inflammation.
8. Describe the chronic inflammatory process.
9. Identify and describe the functions of the cells that take part in chronic inflammation.
10. List the systemic manifestations of inflammation.
11. Define and differentiate between the processes of regeneration and repair.
12. List the sequence of events in the repair process.
13. Identify the major chemical mediators involved in the repair process.
14. Describe healing by primary and secondary intention.
15. List factors that can affect wound healing.
16. List specific ways that tissue can be damaged during the chronic inflammatory process.
17. Identify the complications of wound healing.
18. Describe the clinical characteristics of alveolar osteitis.
19. Describe possible ways to prevent and treat alveolar osteitis.

CHAPTER OUTLINE

Acute Inflammatory Process
- Phases of the Acute Inflammatory Process
  - Initiation Phase
  - Amplification Phase
  - Termination Phase

Cellular Components of the Inflammatory Process
- Granulocytes
- Agranulocytes
- Mast Cells

Chemical Mediators
- Exogenous Chemical Mediators
- Endogenous Chemical Mediators
  - Preformed Chemical Mediators
  - Synthesized Chemical Mediators
  - Plasma-Derived Chemical Mediators
    - The Complement System
    - The Clotting System
    - The Kinin System

Systemic Manifestations of Inflammation

Outcomes of Acute Inflammation
- Chronic Inflammation
  - Granulomatous Inflammation
- Abscess Formation
- Resolution of the Inflammatory Process
- Regeneration
- Fibrous Repair
  - Types of Fibrous Repair
    - Healing by Primary Intention
    - Healing by Secondary Intention
  - Factors That Affect Wound Healing
  - Complications of Wound Healing
- Tooth Extraction: Bone and Soft Tissue Repair

RELATED CLINICAL PROTOCOL

#14 Postoperative Instructions for Oral Surgery Patients

Acute Inflammatory Process

Any time the body is injured by exogenous or endogenous elements, it must respond. The inflammatory process is the mechanism for dealing with injuries caused by these elements. Most of the time the inflammatory process is beneficial, but occasionally, the inflammatory process is ultimately the cause of severe damage and must be held under control. Many immune system diseases (discussed in Chapter 4) are the result of excessive or unnecessary inflammatory processes. There are two broad categories of inflammatory processes, acute and chronic. **Acute inflammation** is most often limited in area and duration and is characterized by the **cardinal signs of inflammation** (Table 3.1). Occasionally, acute inflammation is extensive and involves multiple organs or systems. Chronic inflammation, one possible result of acute inflammation, is characterized by a long duration or a history of repeated insults or injuries. Other outcomes of acute inflammation are abscess formation, **resolution** of inflammation (reversal of the inflammatory process with return to normal), and healing or **repair** of the area. Although the repair process is discussed at the end of this chapter, repair begins at almost the same time the inflammatory process is activated. That is, they occur simultaneously.

TABLE 3.1 Cardinal Signs of Inflammation

Cardinal Sign (Latin Term)	Causative Agent in Inflammatory Process
Redness *(rubor)*	Hyperemia
Heat *(calor)*	Hyperemia
Swelling *(tumor)*	Edema
Pain *(dolor)*	Edema and chemical mediators
Loss of function *(functio laesa)*	Edema

Phases of the Acute Inflammatory Process

There are three phases of the acute inflammatory process. The first phase, or initiation, is activated when the injury occurs. It comprises changes to the structure of small blood vessels (**microcirculation**) in the area of the injury, leading to loss of fluid from the blood and movement of white blood cells from the blood vessels to the injured area. The second phase (amplification) involves the action of chemical substances that direct more and different types of white blood cells into the injured area. The white blood cells act to increase the response, quickly neutralize whatever caused the injury, and clean up the debris resulting from the injury. The third phase (termination) requires other chemical substances to stop or inhibit the inflammatory process; if the inflammatory process continues unhindered, more damage than the initial injury will result.

Understanding the inflammatory process requires an understanding of events occurring within the tissues on a microscopic level and the stimuli causing these events. Table 3.2 provides a list of the main events occurring in this process, and Figure 3.1 illustrates the events at the microscopic level. The following is an example of the acute inflammatory process as discussed in Table 3.2.

Imagine working in the backyard, cleaning up debris from a hard winter. It is so wonderfully warm you have taken off your shoes to go barefoot. Before long, you step on a rusty nail. Your first reactions are to yell with pain and pull the nail out. The following is a description of how your body reacts on a microscopic level.

TABLE **3.2** **Summary of the Acute Inflammatory Process**

Event	Stimuli	Description
1. Vasoconstriction	Injured nervous tissue	Brief hemorrhage control
2. Vasodilation	Histamine Platelet-activating factor (PAF) Bradykinin Prostaglandins (late)	Increases diameter of vessels Hyperemia (increased blood in the area)
3. Increased vascular permeability	Histamine Serotonin PAF Bradykinin Prostaglandins (late) Leukotrienes (late)	Causes gaps in vessel wall between endothelial cells Begins process of exudate formation and vascular stasis
4. Vascular stasis a. Margination b. Adhesion c. Transmigration	Increased vascular permeability Increased blood viscosity Tumor necrosis factor Interleukin-1 Complement	Increases blood viscosity Leukocytes move to the endothelial walls and begin the process of rolling Leukocytes stick to the vessel walls Leukocytes squeeze through gaps in endothelial cells
5. Chemotaxis	Leukotrienes Chemokines Complement	Drives polymorphonuclear neutrophils and other leukocytes to the affected area
6. Opsonization	Immunoglobulins Complement	Prepares resistant pathogens for phagocytosis
7. Phagocytosis	PAF	Enables ingestion and digestion of foreign material or cellular debris
8. Termination of process		Removes debris through lymphatic system

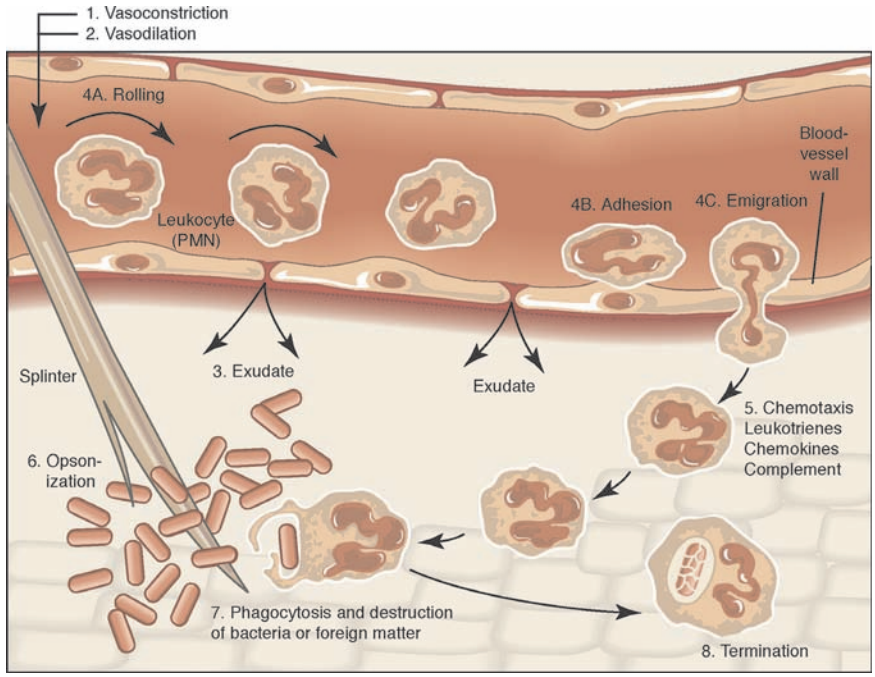

FIGURE 3.1. Summary of the acute inflammatory process (refer to Table 3.2). **1. Event 1, Vasoconstriction.** Following the injury, a brief vasoconstriction may help control bleeding. **2. Event 2, Vasodilation.** Chemical mediators released by the injured cells cause dilation of the blood vessels immediately after the vasoconstriction. **3. Event 3, Increased vascular permeability.** Increased vascular permeability allows plasma fluid (exudate) to leave the vessels and the blood flow to slow, causing vascular stasis. **4. Vascular Stasis. Event 4A, Margination.** Leukocytes (polymorphonuclear neutrophils [PMNs]) move to the vessel walls and begin the process of rolling. **Event 4B, Adhesion/Pavementing.** Leukocytes (PMNs) stick to the vessel walls. **Event 4C, Emigration/Transmigration.** Leukocytes (PMNs) squeeze through the gaps in the endothelial cells. **5. Event 5, Chemotaxis.** Chemical mediators released by the injured cells and bacteria drive leukocytes (PMNs) toward the area of injury. **6. Event 6, Opsonization.** Opsonins prepare resistant microbes and/or other matter for phagocytosis, if necessary. **7. Event 7, Phagocytosis.** Microbes or other matter are phagocytized and digested by the leukocytes (PMNs). **8. Event 8, Termination.** Leukocytes remove digested matter through the lymph system.

Initiation Phase

The first reaction during initiation is an immediate constriction of the microcirculation comprising the arterioles, capillaries, and venules known as **vasoconstriction** (Event 1). The constriction is very brief, lasting several minutes or less, but it serves the purpose of controlling bleeding, especially in small injuries. When tissue cells are damaged, as the cells of the foot in this situation, they release substances called **chemical mediators** that start the inflammatory process. Their first action is to cause the blood vessels in the area to undergo **vasodilation** (Event 2), or increase in diameter, so more blood (**hyperemia**) and nutrients can be brought into the area. Some chemical mediators cause blood vessels to become more **permeable** (Event 3) as cells in the capillaries separate slightly, forming microscopic gaps between them. This allows **plasma fluid** and white blood cells in the vessels to travel out of the vessels and into the injured area. The plasma fluid and white blood cells clear the area of dead or injured cells and any foreign material that entered along with the nail.

At this point, your foot is becoming red, warm to touch, and swollen around the injury. The increased blood flow (Event 2) causes redness and heat, and the plasma fluid flowing out of the more permeable vessels (Event 3) causes the swelling. Heat, redness, and swelling are all cardinal signs of inflammation. The plasma fluid flowing into the injured tissue is called **exudate**. There are several types of exudate; in this case, **serous exudate** is present. Table 3.3 gives a description of the different types of exudates. The exudate contains additional chemical mediators that enhance the inflammatory process. It also contains nutrients to maintain white blood cells called to the area by these chemical mediators. Exudates dilute and neutralize toxic substances. A large amount of exudate within tissues is known as **edema.**

As plasma fluid is lost into the injured area, the blood in the vessels becomes thicker or more viscous. This results in **vascular stasis** (Event 4) or slowing of the blood through the vessels in the affected area. Vascular stasis allows more nutrients to be removed from the blood and brought into the tissues, but it also allows the blood to become stagnant and slows the removal of waste products. Vascular stasis allows the next step in the inflammatory process to begin.

TABLE **3.3** Types of Exudate

Type of Exudate	Description	Example
Serous	Thin and clear Few cells	Blisters from a second-degree sunburn
Purulent or suppurative (commonly called "pus")	Somewhat thick and white or yellowish Many polymorphonuclear neutrophils	Pustules of acne Periodontal abscess

Slower blood flow causes the red blood cells to move toward the center of the blood vessel, while white blood cells, or **leukocytes,** move to the lining of the vessels or the **endothelium.** The move toward the endothelial cells is called **margination** (Event 4A). As they move, they bounce against the endothelial surface, causing them to start rotating. This motion is referred to as rolling. Rolling exposes the surface of the white blood cell to the endothelium, activating the white blood cell so that it can stick to the endothelium in a process called **adhesion** or **pavementing** (Event 4B) (Fig. 3.2). When the white blood cells attach firmly to the endothelial cells, they squeeze through gaps between the cells in the vessel wall created when the vessel became more permeable. This process is called **transmigration** or **emigration** (Event 4C) (Fig. 3.3). After leaving the blood vessels, the leukocytes migrate to the injured area by following a chemical pathway in a process known as **chemotaxis** (Event 5). Chemotaxis results from the action of chemical mediators released by cells damaged during the initial injury that "drive" the leukocytes to the injured area like an emergency beacon calling rescue workers. The leukocytes are prepared to destroy and remove foreign substances and dead or injured host cells.

Amplification Phase

The amplification phase begins as the first leukocytes gather around the injury. When the nail entered the foot, it brought microorganisms and bits of dirt and rust with it. All of this foreign matter will need to be removed from the tissues. Many pathogenic organisms have defense mechanisms making them difficult to destroy and remove from the area. **Opsonization** (Event 6) enables leukocytes to destroy and remove these resistant organisms. The resistant organisms are prepared for destruction by chemical substances called **opsonins** found in exudate collecting within the injured area. **Immunoglobulins,** natural antibodies produced by the immune system, are an example of one type of opsonin. If opsonization is necessary, organisms will be coated with opsonins to prepare them for removal by the leukocytes. Foreign matter is eliminated by leukocytes during a process called **phagocytosis** (Event 7) (Fig. 3.4). If the injury is extensive and there is so much debris it cannot be phagocytized by the leukocytes, the inflammatory process will be amplified further by more chemical mediators, and different types of leukocytes will be called into action from the surrounding tissue and blood vessels.

Termination Phase

During the termination phase, foreign material and cellular debris resulting from the injury and the inflammatory process will be removed through the lymphatic system (Event 8). Other chemical mediators will inhibit or stop further action by the inflammatory process, and the area will complete the healing or repair process. If the inflammatory process is not halted for some reason, the process will become long term, resulting in more damage to the tissue instead of healing.

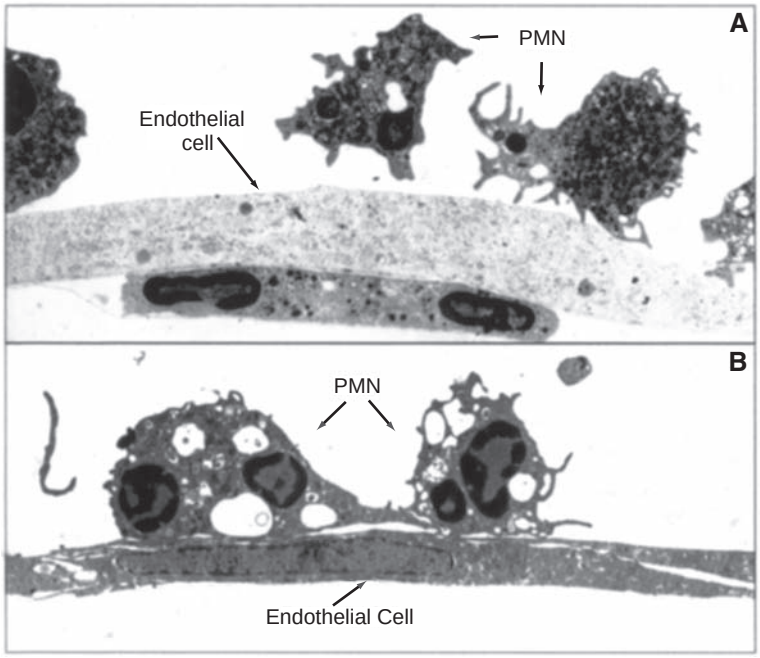

FIGURE 3.2. Adhesion. **A.** The surface of a polymorphonuclear neutrophil (PMN) is exposed to chemical mediators on and near the surface of the endothelial cells as it rolls along the endothelial surface. **B.** The chemical mediators enable firm adhesion of the PMN to the endothelial cell surface. (From Rubin E, Farber JL. Pathology. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2005.)

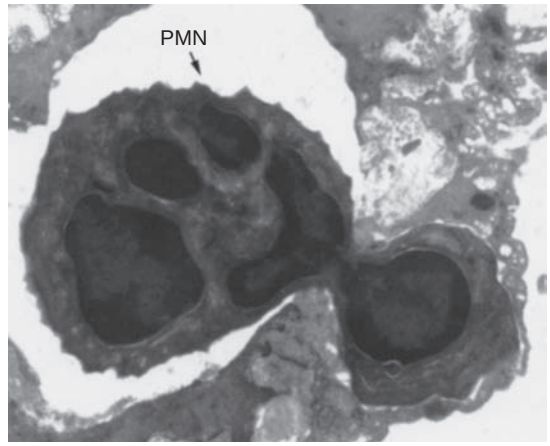

FIGURE 3.3. Leukocyte emigration/transmigration. The polymorphonuclear neutrophil is exiting through the gap in the endothelial cells. (From Rubin E, Farber JL. Pathology. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2005.)

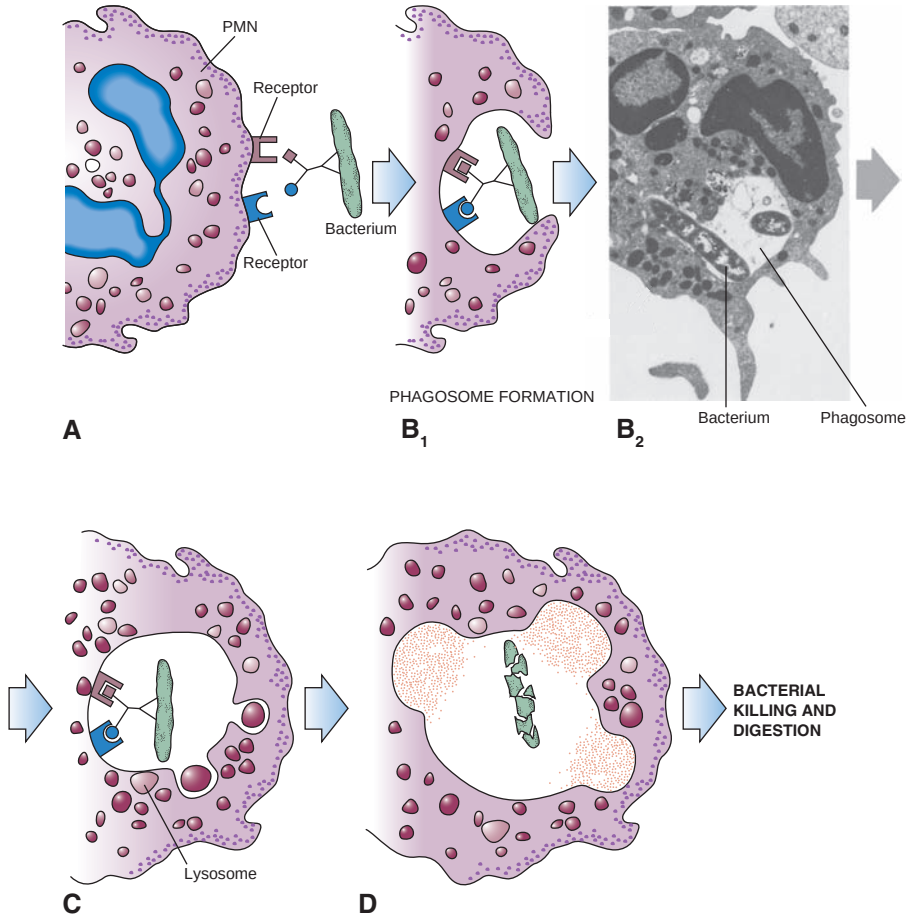

FIGURE 3.4. Phagocytosis. This polymorphonuclear neutrophil (PMN) is phagocytizing a bacterium (long rod-shaped structure). **A.** The PMN captures the bacterium. Receptors on the surface of the PMN are attracted to substances (opsonins) on the surface of the bacterium. **B1.** The PMN forms a phagosome around the bacterium. **B2.** Micrograph of an actual phagosome containing a long rod-shaped bacterium. **C.** Lysosomes fuse with the surface of the phagosome and release lysosomal enzymes into the phagosome. **D.** The bacterium is destroyed and digested by the PMN. (From Rubin E, Farber JL. Pathology. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2005.)

The "nail-in-foot" scenario describes how the inflammatory process is carried out by both cellular and chemical components. These components are described below in more detail to examine how they are interrelated.

Cellular Components of the Inflammatory Process

The main cellular components of the inflammatory reaction are white blood cells or leukocytes as seen in Figure 3.5. Each type of leukocyte plays a vital role in accomplishing the actual work done during the inflammatory process. Leukocytes are divided into two major classes, **granulocytes,** including polymorphonuclear neutrophils (PMNs), eosinophils, and basophils, and **agranulocytes,** including lymphocytes and monocytes. Lymphocytes or lymphoid cells play a specific role in the immune system and are discussed in Chapter 4. Mast cells also play a role during the inflammatory process. The **mast cell** is not a leukocyte but exhibits some of the same properties as the basophil. The mast cell is very important to the immune system (see Chapter 4), and because the immune system plays an important role in the inflammatory process, the mast cell is included in this list.

Granulocytes

The **polymorphonuclear neutrophil** is the most active granulocyte in the inflammatory process. The PMN follows an elaborate plan to eliminate or neutralize the initial cause of the inflammatory process, whether it is foreign material, microbes, or injured host cells that no longer function correctly. PMNs are **motile phagocytes** that can move independently within tissues to phagocytize whatever material they are sent to eliminate. The PMNs are attracted to an area by chemotactic factors and are active in fighting bacterial and fungal infections. It is important to remember they are the first cells to arrive in an area of acute inflammation.

Basophils and **eosinophils** play a role in inflammation related to allergic reactions. In addition, eosinophils are active in fighting off parasitic infections, especially of the helminthic (tapeworm) type.

Agranulocytes

While granulocytes are active during the initial stages of inflammation, the agranulocytes are more active during the later stages of the acute inflammatory process. Agranulocytes are longer-lived (i.e., several months as opposed to 6 to 9 hours) and much slower to respond to the direction of chemical mediators. There are two types of agranulocytes: monocytes (macrophages) and lymphocytes.

Monocytes circulate within the bloodstream until they enter a specific tissue and become "fixed." The "fixed" monocyte differentiates into a **macrophage** specific for that particular tissue. There are many different types of macrophages: a monocyte fixed in the liver is called a Kupffer cell; if it is fixed in the brain it is called a microglial cell. A monocyte fixed in connective tissue becomes a histiocyte, or tissue macrophage. Histiocytes are very important not

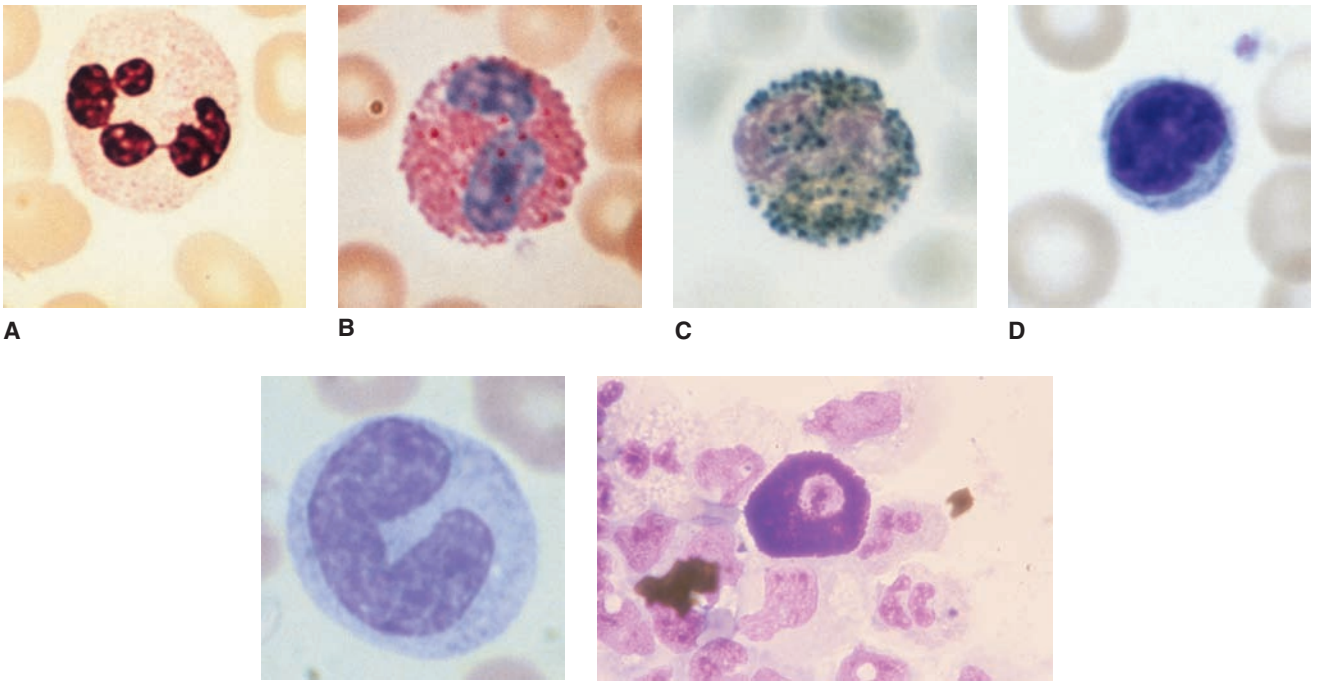

FIGURE 3.5. Cells that take part in the inflammatory process. **A.** Polymorphonuclear neutrophil. **B.** Eosinophil. **C.** Basophil. **D.** Lymphocyte. **E.** Monocyte. **F.** Mast cell. (From Rubin E, Farber JL. Pathology. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2005.)

BOX 3.1 Macrophage Functions

1. Removal of dead and dying cells
2. Removal of damaged tissues
3. Removal of inhaled particles
4. Removal of foreign bodies
5. Primary defense against some microorganisms, for example, *Mycobacterium tuberculosis*
6. Antigen processing for presentation to T cells (see Chapter 4)

only for the inflammatory process but also for the immune system as a whole. Macrophages are able to introduce foreign substances to the immune system, providing a cellular link between the inflammatory process and immunity (see Chapter 4). Box 3.1 lists the functions of macrophages.

If the material to be removed is too large for a single macrophage, or the microbe is highly resistant to phagocytosis, several will join together to form a **giant cell** (Fig. 3.6). Giant cells digest larger matter or destroy resistant microbes, such as the fungus *Candida,* because together they produce a more highly toxic enzyme than a single macrophage can. A giant cell formed in response to foreign material is called a foreign body giant cell. Langhans giant cells are formed in response to a tuberculosis infection, and Aschoff cells are formed during rheumatic fever.

Lymphocytes are leukocytes found in the lymph system. Lymphocytes play a central role in the function of the immune system and are discussed in detail in Chapter 4.

Mast Cells

The mast cell is not a leukocyte. It is created in the bone marrow and then travels through the circulatory system to a tissue site where it matures. The mast cell stays in connective tissue close to vessels of the circulatory system and epithelial tissues of the integumentary system including the respiratory and gastrointestinal tracts. Both the mast cell and the basophil have granules in their cytoplasm containing **histamine,** an important chemical mediator. Histamine is released when

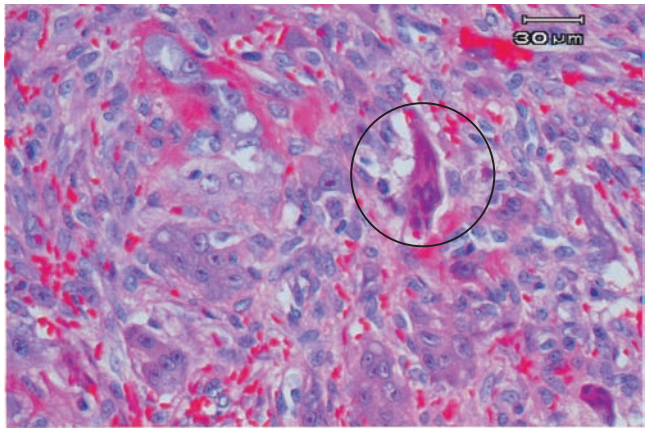

FIGURE 3.6. Giant cell. Note the large multinucleated giant cell in the center of the photo. (Courtesy Yi-Shing Lisa Cheng.)

BOX 3.2 Stimuli That Cause Degranulation of Basophils and Mast Cells

1. Mechanical trauma
2. Heat
3. Ultraviolet radiation
4. Bacterial and fungal toxins
5. Elements of the complement system
6. Enzymes released by injured cells
7. Substances released from polymorphonuclear neutrophils
8. Specific allergens

the cell's granules break open, or degranulate, in response to a stimulus. Box 3.2 lists stimuli that will cause degranulation or release of histamine from basophils and mast cells.

Chemical Mediators

Chemical mediators are molecular substances that direct the actions of cells that take part in the inflammatory and other processes. Chemical mediators recruit cells into an area of injury and determine what specific action is required of them, where the action will take place, and how long the action will be maintained. Chemical mediators can be either exogenous (produced outside of the body) or endogenous (made within the body).

Exogenous Chemical Mediators

Exogenous chemical mediators include the toxins produced by bacteria or created when bacteria are destroyed. For example, **lipopolysaccharide (LPS),** a component of all gram-negative bacterial cell walls, is released when gram-negative bacteria are destroyed. LPS is an important chemical mediator associated with the chronic inflammation seen in periodontal disease. Chemical irritants, such as the substance released into tissues when a mosquito bites or the oil from a poison ivy plant, are also considered exogenous chemical mediators.

Endogenous Chemical Mediators

Endogenous chemical mediators are produced by the body. These chemicals can be produced by a complex sequence of events that activates an inactive form of a substance or precursor circulating in the blood plasma. They can also be produced by specific cells carrying preformed chemicals in intracellular storage areas to be secreted when needed, such as the granules in mast cells, or the cells may synthesize and secrete the chemicals when told to do so by other chemical mediators without storing them within the cell. Endogenous mediators can be divided into three categories: preformed, synthesized, and plasma-derived.

Preformed Chemical Mediators

Histamine, a preformed chemical mediator, is found in the granules of mast cells and basophils and is also released from platelets. Histamine is responsible for dilation of blood vessels and the increase in vascular permeability seen

in the first phases of the inflammatory process. Histamine also causes smooth muscle contraction in the lungs and gastrointestinal tract and stimulates nasal mucus production, all of which are important in allergic reactions. See Chapter 4 for a detailed discussion of the role of histamine in allergic reactions.

Serotonin is a preformed chemical mediator released from platelets in response to platelet-activating factor (PAF) (see below). Serotonin increases vascular permeability just as histamine does.

Synthesized Chemical Mediators

Platelet-activating factor is derived from the cell membranes of neutrophils, eosinophils, basophils, mast cells, monocytes, platelets, and endothelial cells. PAF causes aggregation (sticking together) of platelets and release of serotonin from platelets. PAF is a potent chemical and can increase vasodilation and vascular permeability 100 to 10,000 times more than histamine alone can. PAF also interacts with **phagocytes** such as neutrophils and monocytes/macrophages to increase their phagocytic action.

Prostaglandins are synthesized by all types of leukocytes in response to a stimulus. The prostaglandins cause vasodilation, increased vascular permeability, and increased feelings of pain. They also cause bronchoconstriction and smooth muscle contraction and play a part in elevating body temperature. The prostaglandins are responsible for the sustained effects of vasodilation and vascular permeability seen in later stages of inflammation. In addition, prostaglandins are associated with the tissue destruction seen in periodontal disease.

The **leukotrienes** are synthesized by all types of leukocytes and mast cells. Leukotrienes increase vascular permeability and act as chemotactic agents to bring inflammatory cells into an area. Along with the prostaglandins, leukotrienes are responsible for the sustained effects of vasodilation and vascular permeability seen in later stages of inflammation.

Cytokines are produced by macrophages and some types of lymphocytes. Examples of cytokines active in the inflammatory process are chemokines, tumor necrosis factor, and interleukin-1. The **chemokines** are very strong chemotactic agents for cells involved in the inflammatory process. **Tumor necrosis factor (TNF)** and **interleukin-1 (IL-1)** have numerous effects during all stages of the inflammatory process. They produce fever, increase need for sleep, and decrease appetite. TNF and IL-1 also increase leukocyte adherence, prostaglandin synthesis, and fibroblast production. These substances are also involved with the tissue destruction that occurs in periodontal disease.

Plasma-Derived Chemical Mediators

Three major plasma protein systems are involved in mediation of the inflammatory process. These systems include the complement system, the clotting system, and the kinin system. These systems consist of a series of inactive enzymes. Once the first enzyme in a series is activated, it initiates the next in a series of reactions in which the product of the last reaction is the initiator of the next reaction. This type of process is called a **cascade.**

The Complement System. Activation of the complement system is important in both the inflammatory process and in immunity. The **complement system** comprises a complex series of reactions between plasma proteins. The end product of this cascade, a substance called the **membrane attack complex (MAC),** actually punches a hole in the cell membrane of microbes targeted for destruction by the immune system. Other substances produced in the cascade influence events in the inflammatory process, including vascular effects, leukocyte activation, adhesion and chemotaxis, and enhancement of microbial phagocytosis. In addition, products of the complement system cause mast cells to release their histamine (vascular effects). Other products cause leukocytes to become more active and increase adherence to endothelial cells. Substances that enhance the action of leukocytes are also very strong chemotactic agents stimulating leukocytes to travel to an injured or compromised area. Still another product of the complement cascade is a type of opsonin that attaches to microbial cell walls making them easier to phagocytize (opsonization).

The complement cascade can be triggered by two different pathways, the classic and the alternative pathway. The **classic pathway** is triggered, or started, by antibodies created specifically for the agent causing the inflammatory process. This pathway requires production of a specific antibody for the offending agent and can take time. The **alternative pathway** can be triggered by bacterial LPSs or aggregates (clumps) of preformed immunoglobulins already circulating through the body. The alternative pathway is of much greater importance in an immediate inflammatory process because no time is needed to produce a specific antibody.

The Clotting System. The **clotting system** cascade is activated when a plasma protein called the Hageman factor comes in contact with cellular debris from an endothelial or vessel injury. Although best known for its blood clotting effects, which will be involved in the repair process, the clotting system is involved in activation of both the kinin system and the complement system. Thus, the clotting system is an important factor in the inflammatory process.

The Kinin System. Activation of the **kinin system** cascade results in the formation of the chemical mediator **bradykinin.** Bradykinin is capable of causing vasodilation, increased vascular permeability, and pain. The kinin system is activated by the same substance that activates the clotting system (Hageman factor).

Now that more details have been provided regarding the elements of the acute inflammatory process, refer back to the "nail-in-foot" scenario and replace some of the broader terms such as "chemical mediators" with the names of the specific chemical mediator involved in the action. The same can be done with the broader term "leukocytes." Table 3.2 can be used to complete this exercise. In addition to a localized reaction, you may see systemic manifestations of inflammation in some cases.

Systemic Manifestations of Inflammation

The systemic manifestations of inflammation help control the injury and encourage removal of offending agents and debris associated with the inflammatory process. Systemic manifestations also help start the repair process. Systemic involvement depends on the extent of the inflammatory process and how long it has been present, among other factors. It does not occur every time the inflammatory process is initiated.

One of the hallmarks of systemic involvement is fever, or **pyrexia.** Common **pyrogens,** chemical agents that cause pyrexia, include cytokines produced by leukocytes during the inflammatory process and some of the substances released by bacteria. Pyrogens stimulate the production of prostaglandins, which activate the thermoregulatory center in the hypothalamus, thereby causing an elevation in temperature. An elevated temperature can be important because many pathogens have a very narrow temperature range within which they operate, and even a slight rise in temperature may help destroy them. In addition, small elevations in temperature have been shown to increase the activity and motility of white blood cells and enhance the immune system response. Pyrexia can also be caused by noninfectious agents. For example, pyrexia can be caused by excess thyroid hormones, severe dehydration, and cancer.

Leukocytosis, an increase in the number of white cells in the blood, is another systemic effect of inflammation. Normal white blood cell counts range from 4,000 to 10,000 per mm^3; however, during leukocytosis, white blood cell counts increase up to 100,000 per mm^3. Neutrophils or PMNs increase in number in bacterial infections, in inflammatory disorders, and in response to certain drugs. Lymphocytes are the primary responders in viral infections, and monocytes predominate in chronic infections.

The lymphatic system is important in draining the edema fluid or exudate and clearing the cellular debris and foreign matter from the affected area. Lymphadenopathy, enlargement of the lymph nodes, is another common systemic manifestation of the inflammatory process. The lymph nodes become enlarged, firm, and tender. In localized lymphadenopathy, one or more nodes in the area of the infection or inflammation become swollen and tender, such as when a streptococcal throat infection causes the cervical lymph nodes to become involved. In generalized involvement, nodes all over the body become swollen and tender, for example, the persistent generalized lymphadenopathy (PGL) seen in HIV infection (see Chapter 22). The lymphatic system is responsible for removing all waste products from the inflamed area before healing can begin. If this cannot be accomplished, or if for some other reason the inflammatory process cannot be halted, the reaction will progress to a chronic phase.

Outcomes of Acute Inflammation

The end result or outcome of acute inflammation depends, in part, on the cause of the inflammation. Acute inflammation not associated with tissue damage may progress to chronic inflammation or may resolve completely. Inflammation associated with tissue damage, whether traumatic or not, may progress to chronic inflammation, abscess formation, resolution of the inflammatory process, and healing by either regeneration or repair (Fig. 3.7). Researchers are currently examining the impact chronic inflammation might have on systemic diseases.

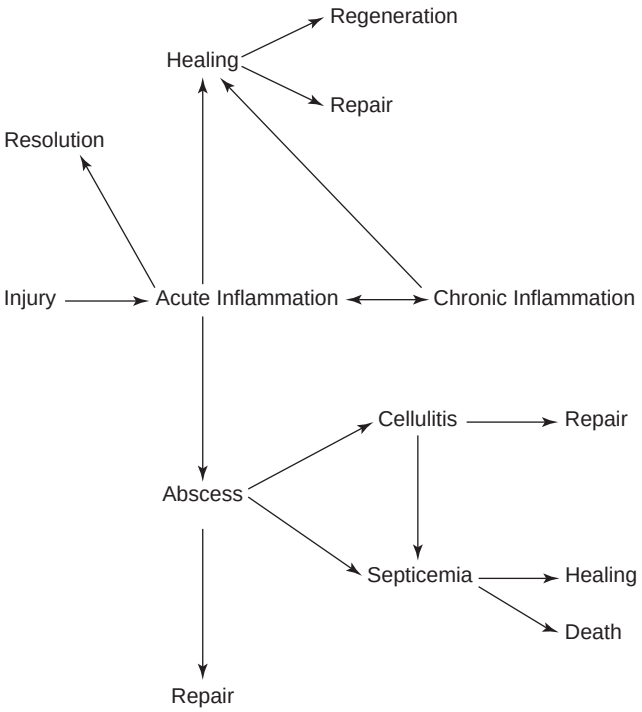

FIGURE 3.7. Outcomes of the acute inflammatory process. This flowchart shows the possible outcomes of acute inflammation.

Chronic Inflammation

It is often difficult to determine when the acute inflammatory process ends and the chronic inflammatory process, one of the possible results of acute inflammation, begins. Acute inflammation should resolve in about 2 weeks. Anything lasting longer than 2 weeks is most likely chronic. The purpose of chronic inflammation is to contain or remove a foreign substance or pathologic agent the acute inflammatory process failed to remove. However, chronic inflammation can occur without a preceding acute stage, as may occur in some autoimmune diseases discussed in Chapter 4. Chronic periodontitis may also occur without a preceding acute inflammatory process. Chronic inflammation is characterized by a large number of mononuclear cells in the tissue, tissue destruction, and ongoing unsuccessful attempts by the tissue to heal.

The major cells seen in chronic inflammation are macrophages, lymphocytes, and, less frequently, plasma cells. Macrophages are driven to the inflamed area by chemotactic agents released by neutrophils already working in the area and by chemical mediators released by

APPLICATION **3.1**

The Oral Systemic Link and Inflammation

Although periodontal disease has been studied for decades, the connection between oral health and systemic health has recently sparked considerable attention. Periodontal disease is recognized as a chronic inflammatory condition; it is, therefore, reasonable to think it may also be associated with other inflammatory diseases or conditions. Many of the same proinflammatory mediators found in periodontal disease may be found in other inflammatory diseases/conditions. These mediators include cytokines such as tumor necrosis factor-alpha (TNF-α), interleukins such as interleukin-1 beta, interleukin-6, interleukin-8 (IL-1β, IL-6, IL-8), chemokines, C-reactive proteins (CRP), and prostaglandins (PGE_2), to name a few. Enzymes produced by periodontal pathogens have also been implicated.

Researchers have studied periodontal disease and its possible relationship to cardiovascular disease (CVD), respiratory diseases, diabetes, rheumatoid arthritis, obesity, chronic renal disease, Alzheimer disease, osteoporosis, and preterm and low birth weight babies. What are the connections?

CVD studies have shown that proinflammatory markers are predictive of recurrent myocardial infarction (heart attack), recurrent stroke, and death due to CVD. The strongest evidence for predicting CVD can be found in increased CRP levels. Studies of respiratory diseases, of which there are a number of subtypes, have found cytokines and enzymes from inflamed periodontal tissues may be aspirated into the lungs where they stimulate local inflammation. Systemic inflammation has been associated with both type 1 and type 2 diabetes mellitus. High levels of circulating CRP are found in individuals with long-term diabetes. Rheumatoid arthritis is associated with an abundant release of cytokines and other proinflammatory mediators similar to those found in periodontitis. Obesity is another condition that may be associated with inflammation. Fat cells have been known to secrete inflammatory cytokines, so it is possible similar pathways may be involved in the pathophysiology of both obesity and periodontitis. The presence of periodontal pathogens in the blood may result in compromised renal function. The development and progression of Alzheimer disease may also be influenced by long-term systemic infections, including oral infections such as periodontal disease, which may cause the cells of the central nervous system to react in an atypical manner resulting in a diseased brain. Osteoporosis or low bone mineral density (BMD) or loss of BMD may be related to more rapid alveolar bone destruction in periodontal disease because the bone is weakened to begin with. Systemic factors affecting bone remodeling in general may also alter local tissue responses to periodontal infection, causing greater and faster bone loss. Elevated concentrations of CRP associated with systemic inflammation have also been associated with adverse pregnancy outcomes (preterm and low-birth-weight babies).

Though the results of some studies suggest an association between inflammatory periodontal disease and other inflammatory diseases/conditions; other studies have found no association. As a result of this ambiguity, meta-analyses and systematic and critical reviews have begun to appear. Most often research has shown or suggested that an association between periodontal disease and the disease in question exists, but it is unclear and they stop short of reporting a causal relationship. Most reports suggest additional studies are necessary, at both the basic and clinical level, to fully explain the relationship between periodontal disease and other inflammatory diseases/conditions. Until research has clarified the controversy surrounding oral–systemic connections, it is the dental hygienist's responsibility to evaluate information using evidence-based resources before introducing the concepts into practice.

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some lymphocytes. Once there, macrophages secrete chemokines that recruit additional monocytes from the blood vessels to the injured site, where they differentiate into macrophages. Other chemical mediators released by the macrophages stimulate lymphocytes or enhance their actions. Macrophages are so powerful they play the major role in chronic inflammation, often causing significant amounts of tissue destruction while performing their job. Tissue destruction is one of the characteristic features of chronic inflammation.

Lymphocytes are present in all cases of chronic inflammation because almost all agents that cause chronic inflammation are also recognized by the immune system as something it should react against. Lymphocytes initiate the immune process that occurs in conjunction with chronic inflammation. **Plasma cells,** a form of lymphocyte that produces antibodies, are also involved in the immune system response and may be seen in areas of chronic inflammation. Chapter 4 discusses how the immune system functions in conjunction with the inflammatory process. It is important to note that chemical mediators released by lymphocytes can stimulate or enhance the action of macrophages. The simultaneous stimulation of both macrophages and lymphocytes by each other enables the persistence of chronic inflammation.

The tissue destruction seen in chronic inflammation is caused by chemicals released from cells that are attempting to eliminate the offending agent or substance from the area. Many of these chemical substances are found within the **lysosomes** of these cells. Lysosomes are organelles containing strong digestive enzymes, called **lysosomal enzymes,** which are associated with the digestion or elimination of phagocytized foreign matter. When a phagocytic cell traps a foreign substance, it creates an intracellular space or vacuole called a **phagosome** to hold

BOX **3.3**

Factors Contributing to the Development and Maintenance of Chronic Inflammation

1. Infectious agents in the area of inflammation
2. Remains of partially digested organisms in the tissues
3. Foreign material in the inflamed tissues
4. Substances produced by the body as part of an abnormal process, which remain in the tissues (e.g., the urate crystals in gout)
5. Incomplete drainage of an abscess
6. Presence of dead or necrotic tissues in the inflamed area
7. Insufficient stability or too much motion of the injured part
8. Physical or mechanical irritation of the injured part

it in (Fig. 3.4). Chemicals released when the phagosome is being created drive the cell's lysosomes to the surface of the phagosome. The lysosomes fuse with the phagosome and release all of their lysosomal enzymes into it, enabling the digestion of the foreign matter. Problems occur when lysosomal enzymes find their way out of the cells and into the tissues. The enzymes may leak from the cell as it is digesting a foreign substance, or all of the intracellular substances may be released when the cell dies. The lysosomal enzymes can destroy normal cells and collagen fibers in the area. They can also activate osteoclasts, causing bone destruction. Bone destruction that occurs during chronic adult periodontitis is a good example of this process. While these destructive processes are occurring, the tissue is trying to heal itself.

Chronic inflammation has been described as "frustrated healing" by many, because everything needed for repair, such as **fibroblasts** (immature connective tissue cell that can differentiate into cells that produce collagen and other tissues) and small blood vessels, is present in the affected tissues. Chronic inflammation will only resolve when all of the agents causing it are eliminated. Box 3.3 presents a list of factors that can contribute to the development and maintenance of chronic inflammation.

Granulomatous Inflammation

Granulomatous inflammation is a subset of chronic inflammation and is characterized by the formation of granulomas. The **granuloma** comprises large macrophages called giant cells and other chronic inflammatory cells surrounding some type of foreign matter. The purpose of the granuloma is to form a wall around the foreign substance and prevent its spread (Fig. 3.8). A periapical granuloma will form at the apex of a nonvital tooth in response to substances produced by necrotic dental pulp tissue (see Chapter 20). Another example is the granuloma produced in the lung in response to *Mycobacterium tuberculosis*. Granulomas heal only after all the stimuli that initiated the inflammatory process are eliminated. For example, the periapical granuloma will heal after endodontic therapy removes the necrotic dental pulp.

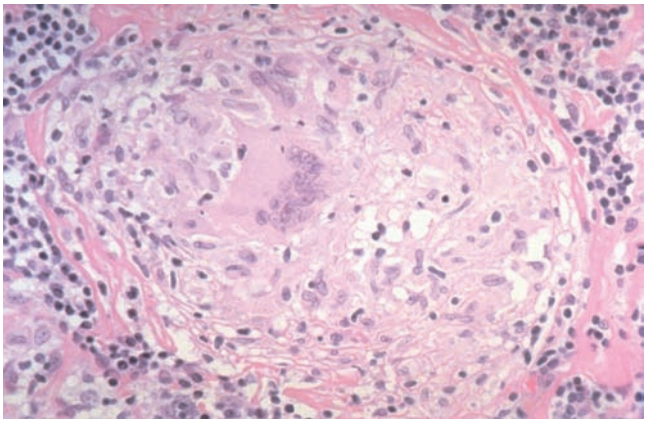

FIGURE 3.8. Granuloma. A high-power photomicrograph of a single granuloma in a lymph node depicts a multinucleated giant cell amid numerous pale epithelioid cells. A thin rim of fibrous tissue separates the granuloma from the lymphoid cells of the node. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

Abscess Formation

Abscess formation occurs when **pyogenic,** or pus-producing, organisms such as staphylococci or streptococci are introduced into the tissues. Pyogenic organisms produce chemical mediators that send out a message for every leukocyte, specifically the PMNs, in the area to come to the site of the injury to consume the organisms. A problem occurs when the pyogenic organisms are resistant to phagocytosis. In this case, the neutrophils die trying to eliminate the organisms, and tissues in the area are destroyed because the neutrophils release lysosomal enzymes when they die. All of the resulting debris accumulates in the tissues as purulent exudate or pus, forming the abscess. The abscess can cause significant damage if not treated. A **fistula** can form through soft or hard tissues. Fistulas occur when enzymes that are released by macrophages literally bore a hole through the tissues along the path of least resistance, ultimately allowing the purulent exudate to exit one area and flow into another or find a path to an outer surface. An example of this is a parulis, which is created when an abscessed tooth forms a fistula tract to the surface of the oral mucosa (Fig. 3.9).

Another sequela involves the spread of bacteria into the surrounding tissues, producing an inflammation of the connective tissue called **cellulitis** (Fig. 3.10). **Ludwig angina**, bilateral cellulitis involving the submandibular, submental, and sublingual spaces, is a serious condition causing rapid swelling of the floor of the mouth with elevation and posterior displacement of the tongue. The swelling often results in partial or complete airway obstruction, making Ludwig angina a life-threatening emergency (Fig. 3.11). In some cases, the bacteria enter the blood and produce a **bacteremia,** or bacteria in the blood. This can lead to **septicemia,** or blood poisoning, and several other conditions. One of the more serious and sometimes fatal conditions is the spread of infection to the cavernous sinus, resulting in the formation of a blood clot or cavernous sinus thrombosis. This is not a common

FIGURE 3.9. Abscess. A parulis that forms as a result of a periapical abscess is an example of an outcome of acute inflammation. (From Fleisher GR, Ludwig S, Baskin MN. Atlas of pediatric emergency medicine. Philadelphia: Lippincott Williams & Wilkins, 2004.)

occurrence; however, media reports of children dying from complications of a neglected dental abscess always cause dismay among dental professionals who know how easily these can be prevented. In any case, abscesses need to be treated quickly before any of these conditions can occur.

Resolution of the Inflammatory Process

In many cases, the inflammatory process is not triggered by a traumatic injury or microbial assault. In these cases, because there was no traumatic tissue damage, resolution can take place. When the stimulus that initiated the process, such as pollen in hay fever, is neutralized, the inflammation resolves, and the tissues return to normal. In the case of tissue damage, healing can only be completed when all of the stimuli that initiated the inflammatory process are neutralized or removed.

FIGURE 3.10. Cellulitis. This child had a painful swollen cheek and infraorbital cellulitis caused by an abscessed tooth. (Courtesy of Dr. Debra Weiner; From Fleisher GR, Ludwig S, Baskin MN. Atlas of pediatric emergency medicine. Philadelphia: Lippincott Williams & Wilkins, 2004.)

FIGURE 3.11. Ludwig angina. Pictured is a patient with Ludwig angina. Note the classic swelling and protrusion of the tongue. This patient was in respiratory distress necessitating a tracheotomy to maintain an open airway. Drains are sutured in place to allow purulent exudate to leave the tissues. (Courtesy of Bechara Y. Ghorayeb, MD.)

Regeneration

The most desired outcome of the inflammatory process is **regeneration.** This is the body's attempt to restore itself to its original state. Regeneration occurs when the stimulus that caused the inflammation is completely removed, the vascular system returns to normal, the injured tissue is replaced with the same type of tissues and cells that were damaged, and the area regains full function. Regeneration depends on the type of cell that was damaged and the extent of the injury. The epithelial cells that line the oral cavity will regenerate because they are already constantly replicating themselves to keep the mucosal barrier intact. Liver cells will regenerate. In transplantations, the liver of the donor will completely regenerate, and the part of the liver that is transplanted into the recipient will regenerate to a more normal size. Brain cells, however, are permanent or nondividing cells; therefore, injured brain cells will not replicate. Some of the lost function may be regained by forming alternative pathways through uninjured brain cells, but the cells that were lost will not regenerate. No matter what type of tissue is involved, if the injured area is large enough, regeneration will not be an option.

Fibrous Repair

If regeneration is not possible, then **fibrous repair** will be the final outcome. Fibrous repair results in the creation of a **cicatrix** (scar) that may recreate normal or near-normal tissue formation or architecture but not normal function.

Chronic inflammation inevitably resolves with scar formation. This outcome is related to the extended healing time and to the amount of tissue damage usually associated with chronic inflammation. Repair is one of the primary functions of the immune system. The process of repair, like the inflammatory process, requires many chemical mediators that control the timing of the wound healing. Some of these chemical mediators include cytokines and epithelium-, fibroblast-, and platelet-derived growth factors.

Remember that the process of repair begins as soon as the inflammatory process is initiated. Almost immediately following an injury, a blood clot forms and fills the wound. The clot provides an area where leukocytes can clean the wound of foreign matter and dead or injured tissue cells. As this is occurring, fibroblasts and vascular endothelial cells begin to appear within the clot. The endothelial cells begin to form new blood vessels in a process called **angiogenesis,** and the fibroblasts start to form collagen fibers. The very fragile vascular tissue that is starting to form is called **granulation tissue** (Fig. 3.12). Granulation tissue forms the framework upon and within which fibrous repair takes place. If the wound appears on a surface of the body, such as the skin or buccal mucosa, epithelialization will most likely occur in conjunction with the formation of granulation tissue. During **epithelialization,** epithelial cells from the lower layer of the epithelium at the edges of the wound start to slide down and across the wound surface beneath the scab. These cells eventually meet and unite, forming a basement membrane and normal stratified squamous epithelium. Eventually the vascular granulation tissue becomes less vascular as the fibroblasts create more collagen fibers. In the end, most of the blood vessels in the tissue are resorbed because they are no longer needed to bring nutrients into the area. Fibroblasts disappear, and what is left is a very dense collagenous tissue, or scar, containing very few blood vessels (Fig. 3.13). It is important to note that whenever a scar forms the function of that area of tissue is lost. Loss of function may not be crucial in a small skin wound, but many problems are associated with even small injuries to nervous tissue. Another problem regarding scar formation occurs because the injured tissue will only regain about 70 to 80% of its full strength; in large injuries, this could be very significant.

FIGURE 3.12. Granulation tissue. Granulation tissue is the framework upon which healing tissue repairs itself. The bottom of this extraction site is filled with granulation tissue.

FIGURE 3.13. Fibrous repair. This scar is an example of fibrous repair. (From Weber J, Kelley J. Health assessment in nursing. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

Types of Fibrous Repair

Healing can involve both repair and regeneration, depending on the specific types of tissue and cells that are involved. In the skin and mucous membranes, the epidermal tissues and the blood vessels in the area will regenerate. The dermis or deeper connective tissues will undergo fibrous repair. Healing by primary intention and secondary intention are the main methods whereby surface wounds undergo healing.

Healing by Primary Intention. This type of repair occurs when the margins of the injury are clean and brought together by sutures, bandages, or pressure. The migrating epithelial cells have little distance to travel, and healing may occur with very little or no visible scarring (Fig. 3.14).

Healing by Secondary Intention. Healing by secondary intention occurs when the loss of tissue is significant enough that the edges of the wound cannot be brought together. The process of repair must begin at the base of the injury and proceed from the bottom to the top. Healing by secondary intention will result in scar formation (Fig. 3.15).

Factors That Affect Wound Healing

The type, size, and location of the wound will affect how it heals. A sharp, clean wound will heal faster than tissue that is torn apart. A large wound will heal more slowly than a small wound. A wound that involves tissues around a joint will heal more slowly than one located in a nonmoving area. Likewise, a wound in an area that has constant irritation from clothing will heal more slowly than one that is not irritated by clothing.

Wounds in highly vascular tissue will heal faster than those in nonvascular tissues. For example, a wound in the oral cavity will heal faster than one located on the dermal surface, primarily because of the increased vascular supply. This is because highly vascular tissue is better able to supply the necessary elements for healing than tissue that is less vascular.

Several other local factors play a part in slowing wound healing. Infection will impair the healing process, as will the presence of a foreign object such as a splinter or shard of

APPLICATION **3.2**

A Tale of Two Healings

The following two scenarios illustrate the difference between healing that occurs in a tissue in which cells replicate and that which occurs in a tissue in which cells do not replicate.

Scenario I: Latoya is a first-year dental hygiene student using an anterior sickle scaler on a "real" patient for the first time. She is very nervous, and she is desperately trying to remember everything she should do to remove slightly subgingival calculus from the distal of tooth 25. Latoya gets the side of the tip one-third inserted under the calculus and opens the face of the blade to what she thinks is the correct working angulation. What she doesn't know is that she has mistakenly opened the face of the blade too far, and the opposite cutting edge is impinging on the interdental papilla. Latoya activates a working stroke and to her disbelief, does not remove any of the calculus. Even more disconcerting, when she activated her working stroke, she removed a small portion of the interdental papilla. Although this is traumatic to almost every student the first time it happens, the effect on the patient is very minor. The oral epithelial tissues are made of rapidly dividing epithelial cells, and the area of injury is very small; therefore, the tissue is more or less regenerated and heals back to its normal size and function. Latoya is relieved to see the tissue has returned to normal the next time the patient comes in.

Scenario II: Shawn, a friend of Julian, another dental hygiene student, has gone to a piercing parlor to have his tongue pierced. The next day Julian gets a phone call from a very upset Shawn, who is unhappy because the feeling in his tongue does not seem to be returning. Julian suggests it might just be due to swelling from the inflammatory process triggered by the injury and that Shawn should give it time to heal. Several days later, Shawn is still experiencing a loss of sensation in his tongue and some loss of function. After consulting with his dentist, it is determined a portion of the lingual nerve was most likely damaged during the tongue piercing. The dentist's recommendation is to wait and see if, after time, some of the sensation and function will return, but there is nothing more that can be done. The injury in this case was small, and the lingual nerve was not totally severed. However, nerve tissue is permanent or nondividing, and the scar tissue produced cannot perform the function of the original tissue.

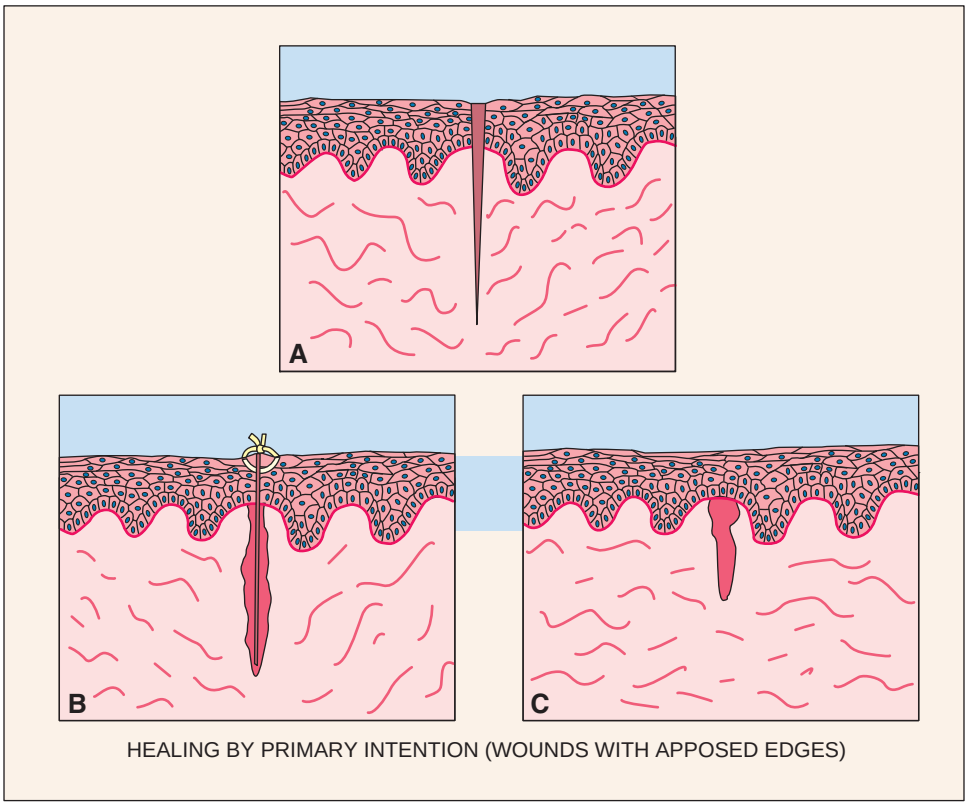

FIGURE 3.14. Healing by primary intention. **A.** There is little loss of tissue in the wound pictured here. In addition, the edges are clean and held closely together by sutures. **B.** This type of damage requires only minimal cell proliferation and the creation of new blood vessels (angiogenesis) to heal. **C.** The outcome of healing by primary intention is a small scar. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

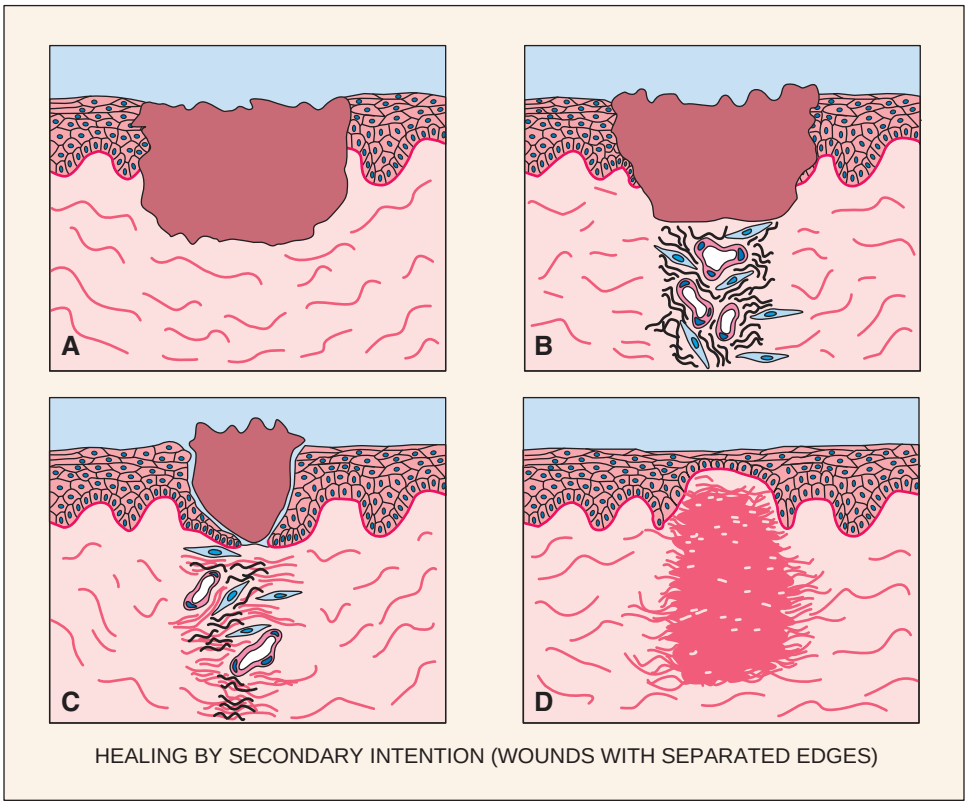

FIGURE 3.15. Healing by secondary intention. **A.** There is substantial loss of tissue in the wound pictured here; the edges are far apart and cannot be drawn together. A blood clot has filled the wound. **B.** Granulation tissue forms within the wound and is the framework upon which the repair process will take place. Endothelial cells migrate into the area and form new vessels (angiogenesis). **C.** Epithelial cells continue to migrate down into and across the wound until they meet, forming the new basement membrane. Fibroblasts create collagen fibers that are deposited within the granulation tissue. **D.** Granulation tissue is eventually resorbed and replaced by the fibrous tissue that forms a large scar that is often functionally and esthetically unsatisfactory. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

glass. Impaired circulation in the area of the wound will delay or prevent healing. This is especially important in older adults and in persons with chronic cardiopulmonary diseases. If an excessive amount of granulation tissue forms in the wound, healing will be delayed because the process of epithelialization will be stopped until the excess tissue is removed.

Systemic factors, such as those occurring in diabetes, can interfere with wound healing. Smokers also have an impaired capacity for wound healing. Many types of nutritional deficiencies, such as starvation, protein malnutrition, and vitamin and mineral deficiencies (especially vitamin C), will delay healing. Healing will be impaired in individuals who have genetic syndromes (see Chapter 6) such as Marfan and Ehlers-Danlos syndromes, which include connective tissue disorders. The systemic effects of certain medications will also impair the healing process. The most important of these are medications that interfere with the inflammatory process or with the immune system, such as corticosteroid, nonsteroidal anti-inflammatory, and other immunosuppressive drugs.

Complications of Wound Healing

The most common complications of healing are inadequate scar formation, excessive scar formation, and excessive contracture of the scar tissue. Inadequate scar formation usually occurs as the result of the production of an inadequate amount of granulation tissue. The most serious result of this is the bursting of a wound after surgery; if a wound bursts after abdominal surgery, there is a 30% chance of mortality (Rubin et al., 2005). Excessive scar formation results in a hypertrophic scar, or **keloid** (Fig. 3.16). These are usually unsightly and tend to recur after removal. The last complication is excessive contracture of the edges of the wound causing extensive deformity, especially if the area is near a joint where limitations in mobility can cause

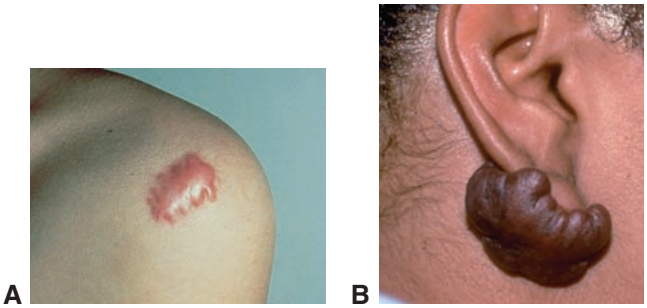

FIGURE 3.16. Keloid. **A.** Keloid on the shoulder. (From Willis MC. Medical terminology: a programmed learning approach to the language of health care. Baltimore: Lippincott Williams & Wilkins, 2002.) **B.** This is an example of excessive scar formation after having the ear pierced. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

FIGURE 3.17. Wound contracture. Deformity caused by excessive contracture of scar tissues after severe thermal burns on the hands. (From Strickland JW, Graham TJ. Master techniques in orthopaedic surgery: the hand. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2005.)

a significant problem. Severe burns often result in wounds that exhibit excessive contracture (Fig. 3.17).

Tooth Extraction: Bone and Soft Tissue Repair

The repair of an extraction site involves most of the same processes discussed above, with slight variation. The acute inflammatory process is triggered by the injury, and PMNs rush into the area. A blood clot fills the extraction site. As stated above, the inflammatory process and the process of repair are occurring at the same time. As the acute inflammatory process continues, the epithelial cells at the edges of the wound begin the process of epithelialization and completely cover the extraction site in about 10 to 12 days. Figure 3.18 shows an extraction site that is almost fully healed. In the meantime, under the surface, osteoblasts from the bone marrow migrate into the clot and begin to produce new bone. The entire area of the extraction undergoes remodeling. The alveolar process is resorbed because it is no longer needed to maintain a tooth and is replaced with spongy bone. The bone is completely filled in by about 12 weeks postextraction. The same conditions that affect soft tissue wound healing, as stated above, will affect bone repair.

FIGURE 3.18. Extraction site. Third molar extraction site is almost fully healed after 5 weeks.

One of the more common problems associated with bone repair in the oral cavity is a dry socket also known as **alveolar osteitis.** This complication is specific to the healing of extraction sites and occurs most often with third molar extractions. Alveolar osteitis occurs when the initial blood clot within the socket is disrupted or lost and the bone surface becomes exposed to the intraoral environment, increasing the risk of infection and causing severe pain. In addition, the exposed bone becomes necrotic and may produce a foul odor. The patient becomes aware of the condition within 2 to 4 days after the extraction. In cases of alveolar osteitis, the necrotic bone must be resorbed by the body, and granulation tissue must form along the walls of the socket instead of within a clot. This process is much slower, often taking several weeks longer than normal. The risk factors associated with alveolar osteitis include excessive trauma to the bone during extraction, tobacco use, and noncompliance with postoperative instructions (Larsen, 1992). Most cases of alveolar osteitis can be prevented by limiting the amount of trauma during the extraction and by the patient complying with postoperative instructions focused on maintaining the integrity of the blood clot. For example, the patient should avoid the following:

- Producing a vacuum in the mouth by drinking through a straw or by smoking for at least 24 hours, because this can dislodge the fragile new clot
- Tobacco use, because this will impair circulation in the area
- Vigorous rinsing for at least 24 hours, because this can also dislodge the clot
- Eating or drinking hot liquids, which might melt the clot

Alveolar osteitis is treated by gently packing strips of a special type of gauze into the socket. The gauze is treated with an antiseptic to reduce the risk of infection and a medication that can soothe the exposed nerves, such as clove oil. In addition, the physical presence of the gauze reduces the chance that food will become lodged in the area. The patient returns every day or two to replace the packing and to check on the healing process until completed (see Clinical Protocol #14).

Conditions and diseases that manifest as inflammatory processes are caused by hundreds of different stimuli, both endogenous and exogenous. Almost every disorder that can be imagined has inflammatory components within its clinical manifestations. The most common diseases and conditions and those that are important in the practice of dental hygiene are discussed in later chapters, where they are addressed within the context of sharing similar clinical manifestations.

SUMMARY

- The acute inflammatory process is carried out by the body using both cellular and chemical mechanisms.
- There are three phases in the acute inflammatory process: initiation, amplification, and termination.

- Initiation involves changes in the microcirculation in which chemical mediators instruct the blood vessels to briefly constrict, then dilate and become more permeable. The vascular changes enable PMNs to emigrate through the endothelial walls into the connective tissue, where they follow the direction of more chemical mediators to the areas where they are needed. In addition, exudate is allowed to flow from the blood vessels into the surrounding area, creating edema.
- Amplification involves gathering all of the necessary cells into the area to phagocytize all of the microorganisms, foreign matter, or other debris that needs to be removed before healing can take place.
- Termination requires shutting down the inflammatory process through the action of other chemical mediators so healing can be completed.
- The complement, kinin, and clotting systems are all involved in mediating the inflammatory process.
- During the process of acute inflammation, systemic manifestations such as pyrexia, leukocytosis, and lymphadenopathy may occur.
- Chronic inflammation may result from unresolved acute inflammation, or it may occur without this stimulus.
- The chronic inflammatory process is controlled by different cells and chemical mediators that attempt to neutralize whatever stimulus is causing the reaction. Continuation of chronic inflammation leads to significant tissue destruction and delayed or abnormal healing.
- Other outcomes of the inflammatory process include abscesses, fistula formation, and cellulitis.
- Chronic inflammation always stimulates an immune system response.
- Tissue regeneration or repair begins at almost the same time as the inflammatory process and continues in conjunction with it.
- Regeneration occurs when the tissue is repaired with the same type of tissue that was lost and the area regains full function. Anything less than this is considered repair.
- Repair of surface wounds occurs by either primary or secondary intention and involves the production of granulation tissue within the wound. Lost tissue is replaced by newly formed connective tissue, and the blood supply is reestablished through the process of angiogenesis.
- Epithelialization replaces the skin covering the wound. The end product is fibrous repair or scar formation.
- Many factors can affect how a wound heals, including the type, size, and location of the wound; the type of tissue involved; and the health status of the individual.
- Keloids, excessive wound contracture, and wound rupture are complications of the repair process.
- Healing of extraction sites involves bone repair and remodeling in addition to soft tissue healing.
- Alveolar osteitis, a common complication following extraction of third molars, can be prevented by reducing the amount of trauma during the surgery, avoiding tobacco use, and following postoperative instruction.

CHAPTER REVIEW

Case Study 3.1

Your patient presents complaining of soreness around the distal of #17. She has not been able to eat on the left side for 2 days and has been taking aspirin for the pain but has had no relief. When you perform your intraoral examination, you see the condition depicted in Figure 3.19.

1. How would you describe your clinical findings?
2. Which cardinal signs of inflammation are present and what has caused them?
3. Which of the cardinal signs of inflammation would be mediated by histamine?
4. What could have caused the inflammation?
5. What can be done to alleviate the condition?

For answers and additional review activities, log in to **thePoint.lww.com**

FIGURE 3.19. Pericoronitis with chemical burn. (Courtesy of Dr. John Jacoway.)

Case Study 3.2

Nineteen-year-old Yulia presented for her dental hygiene appointment with the lesion pictured here (Fig. 3.20). She stated it seemed to start from a tiny pimple on her chin she had "squeezed" 2 days ago. Since then her lip has become swollen and very sore to the point she is unable to eat. She reports no other symptoms. Palpation of the cervical and submandibular lymph nodes finds several enlarged, indurated, and tender nodes in each area.

1. How would you describe your clinical findings?
2. Which cardinal signs of inflammation are present and which event in the inflammatory process caused each one?
3. What is the significance of the enlarged lymph nodes?
4. This is an example of a bacterial infection. Describe how white blood cells move into the area and how they are able to destroy the invading bacteria.
5. Which chemical mediators are involved in chemotaxis and destruction of bacteria?

FIGURE 3.20.

For answers and additional review activities, log in to **thePoint.lww.com**

Critical Thinking Activities

1. What would be the positive and negative aspects of not having an inflammatory process?
2. What do you think would happen if the inflammatory process were to run out of control? How would you attempt to control it?
3. How can you use information you have learned about the inflammatory process to explain gingivitis and periodontitis to your patient?

Portfolio Possibility

- Work with a group or individually and develop a case study that works through all of the steps involved in the inflammatory process. This case can be based on an imaginary injury or something that actually happened to you or someone from your group. Use this case study to review the events and cellular and chemical elements constituting the inflammatory response with the rest of your class or use it to help tutor classmates who are having trouble understanding the information. Keep a copy of the case study for your portfolio; include a reflection about what you learned from the project and how you utilized it to assist others.

Media Menu

Web Sites

Journal of Periodontology: Volume 79, Number 8s, August 2008—Issue focuses on the inflammatory response; all articles in this issue can be accessed free of charge
http://www.joponline.org/toc/jop/79/8s

Centers for Disease Control and Prevention: Bensley L, VanEenwyk J, Ossiander EM. Associations of self-reported periodontal disease with metabolic syndrome and number of self-reported chronic conditions. *Prev Chronic Dis* 2011;8(3).
http://www.cdc.gov/pcd/issues/2011/may/10_0087.htm

Multimedia Resources

Crawling Neutrophil Chasing a Bacterium
http://youtu.be/I_xh-bkiv_c

Histopathology Soft Tissue: Foreign body reaction (foreign body giant cells)
http://youtu.be/CRmwufRisfc

Study Tools

Take advantage of additional online resources to help you study and ace your exams!

- Answers to case studies in the book
- Additional case studies and answers
- Interactive quiz bank with answer feedback
- Fully searchable e-book for quick lookup and studying on-the-go
- Expanded Media Menu with direct links to related Web sites and multimedia resources
- Supplemental references

thePoint Online resources and links are available at http://thepoint.lww.com/DeLong2e

REFERENCES

Larsen PE. Alveolar osteitis after surgical removal of impacted mandibular third molars. Identification of the patient at risk. Oral Surg Oral Med Oral Pathol 1992;73(4):393–397.

Rubin E, Gorstein F, Rubin R, et al. Rubin's pathology: clinicopathologic foundations of medicine. 5th ed. Baltimore: Lippincott Williams & Wilkins, 2008:37–70.

CHAPTER 4

The Immune System and Immunity

KEY TERMS

Acquired immunity
Active immunity
Allergic contact dermatitis (ACD)
Anaphylactic reaction
Angioedema
Antibody
Antigen
Antigen-binding fragment
Antigen-presenting cell (APC)
Atopic reaction
Autoimmune disease
Cell-mediated reaction
Cytokines
Cytotoxic reaction
Graft-versus-host reaction
Haptens
Immune complex-mediated reaction
Immunoglobulin (Ig)
Irritant contact dermatitis (ICD)
Maculopapular
Major histocompatibility complex (MHC)
Memory cell
Natural killer cell
Nonspecific (natural, innate) immunity
Opportunistic infection
Passive immunity
Plasma cell
Primary immune response
Primary immunodeficiency
Secondary immune response
Secondary immunodeficiency
Self-tolerance
Specific immunity
Target cells
T cytotoxic cell
T helper cell
Waldeyer ring

LEARNING OUTCOMES

1. Define and use key terms that describe the immune system.
2. List examples of antigens.
3. Describe the nonspecific immune system.
4. Describe the location and elements of Waldeyer ring.
5. List the immune system cells and their functions.
6. List the names and functions of the major cytokines involved in the immune response.
7. State the ultimate goal of the immune response.
8. Describe and differentiate between humoral and cell-mediated immunity.
9. Discuss how the immune system recognizes, reacts to, and remembers antigenic agents.
10. Describe the characteristics of the five major antibody groups.
11. List the four ways of achieving specific immunity.
12. Discuss and give examples of the four types of hypersensitivity reactions.
13. Identify methods to avoid latex hypersensitivity reactions.
14. Describe the concept of self-tolerance as it relates to autoimmune diseases.
15. Differentiate between primary and secondary or acquired immune deficiency diseases.
16. Describe the impact of immune deficiency on an individual and the role opportunistic infections play in the process.

CHAPTER OUTLINE

Immunity
- Immune System Triggers or Antigens
- Nonspecific Immunity
- Specific Immunity
  - Organs Associated with the Immune System
  - Cellular and Chemical Components of the Immune System
  - The Immune Response
    - Humoral Immunity
    - Cell-Mediated Immunity
    - Types of Specific Immunity

Immunopathology
- Hypersensitivity Reactions
  - Type I (Anaphylactic or Atopic Reactions)
    - Latex Hypersensitivity Reaction
  - Type II (Cytotoxic Reactions)
  - Type III (Immune Complex-Mediated Reactions)
  - Type IV (Cell-Mediated or Delayed Hypersensitivity Reactions)
    - Allergic Contact Dermatitis Associated with the Use of Latex Gloves
    - Irritant Contact Dermatitis
- Autoimmune Diseases
- Immune Deficiency Diseases
  - Primary Immunodeficiency Disease
  - Secondary Immunodeficiency Disease

RELATED CLINICAL PROTOCOL

#6 Treating Patients with Sensitivity to Flavoring Agents

Immunity

The body has many defenses against invaders or substances that can cause disease or injury. The inflammatory process, discussed in Chapter 3, is one of these defense mechanisms. Inflammation is an immediate response that occurs when foreign or injurious agents are allowed into the cells or tissues of the body. Cells and chemical products produced during the inflammatory process are essential in activating another of the body's defenses, the immune system. The goal of the immune system is to prevent foreign substances from entering the body and to establish immunity or resistance to disease-producing agents, such as bacteria and viruses, through the immune response.

Immune System Triggers or Antigens

The agent that triggers the immune response is called an **antigen**. Antigens can be chemicals (natural or synthetic), food proteins, the products of microbes (lipopolysaccharides), the microbes themselves, abnormal human tissue cells, donor tissue cells, or the person's own normal tissue cells. Antigens are usually large-molecular-weight substances, such as proteins and polysaccharides. Smaller-molecular-weight substances, such as some metals, some medications such as penicillin, and the oils produced by some plants like poison ivy, for example, are called **haptens**, and can only exhibit antigenic properties when combined with a larger human protein from the skin, blood, or other tissue. The larger-molecular-weight substances, such as lipopolysaccharides, can trigger the immune response without such help.

Immune system cells need to be able to distinguish self from nonself. The body accomplishes this by "coding" each cell surface with molecules that are the equivalent of an identification tag. These molecular identification tags are called **major histocompatibility complexes (MHC)** and are found on almost every cell having a nucleus. MHCs may also be called human leukocyte antigens (HLAs). The MHCs play an important role in activating the immune response. Any time there is a change in the MHC of a particular cell, caused by injury, viral infection, or other stimulus, the MHC will become antigenic, and the cell will no longer be recognized by the immune system as self. This change initiates the immune response, which results in destruction of the cell. MHCs play a vital role in organ and tissue transplantation. It is important to match the MHC molecules of organ and tissue transplant recipients and their donors as closely as possible to minimize the potential for rejection of the transplant.

Nonspecific Immunity

Nonspecific immunity (sometimes called **innate** or **natural** immunity) comprises defense mechanisms that require no previous exposure to an offending agent to accomplish their objective of neutralizing that agent. Examples of nonspecific immunity include the following:

- Physical barriers
  - Integumentary system (skin and mucous membranes)
  - Waldeyer ring
  - Nasal hairs, sneezing
  - Respiratory tract cilia, coughing
- Chemical barriers
  - pH of the skin
  - Mucous secretions
  - Gastric acids
  - Tears, sweat, and saliva
- Nonspecific phagocytes
  - Monocytes, macrophages, and neutrophils
- Indigenous microbes that compete with pathogens
- Inflammatory response
- Clotting system
- Complement and kinin systems

The inflammatory process, kinin, clotting, and complement systems and the action of some of the phagocytic cells are integral parts of nonspecific immunity. In addition, the

chemical mediators involved in these processes or secreted by the phagocytic cells are essential in activating or enhancing the immune process that eventually results in resistance to specific antigens or specific immunity.

Specific Immunity

Specific immunity (sometimes called **acquired immunity**) is the second form of immunity that, along with the inflammatory, healing and repair processes, helps maintain the body in a healthy state. Specific immunity acts against previously encountered antigens with antibodies and activated lymphocytes specific for that antigen. This is called the immune response, and it is carried out by the immune system.

Organs Associated with the Immune System

The principal organs of the immune system are the bone marrow, thymus, spleen, lymphatic vessels and nodes, and mucosa-associated lymphoid tissues. The bone marrow produces the cells of the immune system from precursor stem cells. The thymus gland educates some of these cells, called T cells, to make them **self-tolerant** (having the ability to recognize the host's own cells as self). The spleen has two functions. It serves as a filter to remove old and damaged red blood cells from the general circulation, and, as part of the immune system, it will mount an immune response against any foreign substance presented to it via the same circulating blood. The lymphatic system can initiate an immune response, process some of the immune system cells (called B cells), and remove foreign substances from the host through a system of vessels and nodes placed throughout the body. Also, numerous strategically placed mucosa-associated lymph tissues are important in maintaining the immune status of the individual by detecting and removing injurious substances before they compromise this defensive barrier. Most of these are located in the gastrointestinal, respiratory, and genitourinary tracts. The most notable in the oral-pharyngeal area is **Waldeyer ring**, which comprises the adenoid or pharyngeal tonsil and the lingual and palatine tonsils (Fig. 4.1).

Cellular and Chemical Components of the Immune System

The immune system consists of chemical molecules and immune cells that inhabit lymphatic tissue and circulate in body fluids. The cells of the immune system include macrophages and lymphocytes. Chapter 3 describes macrophages as they relate to the inflammatory process. This chapter illustrates the role of macrophages in the immune system response, showing how they are an integral part of both processes. The lymphocytes are white blood cells found in lymphoid tissues. Lymphocytes are divided into two categories: B lymphocytes and T lymphocytes. The B lymphocytes are most active in humoral immunity, while the T lymphocytes are most active in cell-mediated immunity, although they are also necessary for the optimal functioning of humoral immunity. Lymphocytes are discussed later in this chapter.

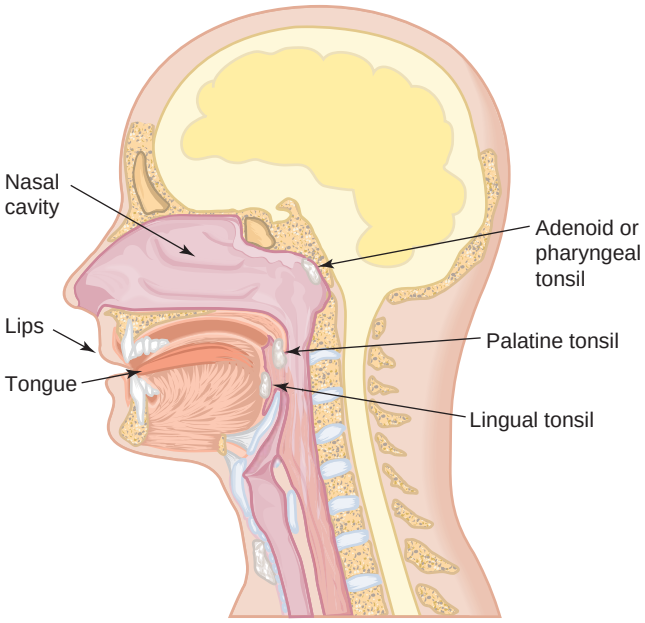

FIGURE 4.1. Waldeyer ring. The lingual and palatine tonsils and the adenoid or the pharyngeal tonsil comprise Waldeyer ring and are important elements of nonspecific immunity that encounter foreign substances as they enter the body through the oral cavity.

A complex system of chemical molecules or **cytokines** produced by the immune cells regulates how the system responds to a stimulus. Cytokines have various functions, such as carrying messages to and from cells, enhancing cell growth, stimulating chemotaxis, and activating immune cells. Table 4.1 lists specific cytokines, their source, target cells, and actions.

The Immune Response

The goal of the immune response is to remove or neutralize antigenic substances. To accomplish this goal, the system must recognize the "invader," react to the invader, and remember the invader. There are two interactive components of this systemic immune response: humoral immunity and cell-mediated, or cellular, immunity.

Humoral Immunity. Humoral immunity is provided by the B lymphocytes or B cells. These cells develop in the bone marrow and then mature in lymphoid tissue throughout the body. The maturation process ensures the surface of each B cell contains **antibody,** that is, molecules that react against one or more specific types of antigen. The **antigen-binding fragment** (Fab) is the part of the antibody that combines with or binds to an antigen (Fig. 4.2). The B cell becomes activated when its antigen-binding fragment comes in contact with an antigen it can bind to. Another type of lymphocyte, the **T helper cell** (discussed in the next section) must also bind to the B lymphocyte before it can become activated. The end product of this activation is the transformation of the B cell into an antibody-secreting lymphocyte known as a **plasma cell**. Both B and T cells

TABLE 4.1 **Cytokines and Their Functions**

Cytokine	Source	Target Cells	Biologic Activities
Interleukin 1 (IL-1)	Lymphocytes Antigen-presenting cells	Monocytes Macrophages Neutrophils Osteoclasts Fibroblasts	Chemotactic factor for monocytes and neutrophils Induces fever and other systemic manifestations Increases bone resorption Induces fibroblast proliferation
Interleukin 2-8 (IL2-8)	Activated T cells Mast cells	Macrophages T cells B cells Mast cells Natural killer (NK) cells	Chemotactic factor for macrophages and neutrophils Promotes growth of B and T cells Growth factor for mast cells and NK cells Enhances activation of cytotoxic T cells
Tumor necrosis factor	Macrophages Activated T cells	Monocytes Neutrophils Tumor cells	Mimics actions of IL-1 Cytotoxic to select tumor cells Activates phagocytic cells
Interferon	Leukocytes Fibroblasts Activated T cells	NK cells Viruses Macrophages Endothelial cells	Induces NK activity Activates macrophages Antiviral activities Activates endothelial cells

must function together before a plasma cell can be created and antibodies produced. Plasma cells live for only a few days. The process of B cell activation also stimulates the plasma cells to divide and become more numerous, which increases the amount of antibody produced. In turn, the bone marrow is stimulated to produce more B cells that can become plasma cells upon activation. It takes about 2 to 3 weeks to build up enough circulating antibody to inactivate most antigens after this initial exposure. This process is called the **primary immune response**. The slow production of antibody at the initial exposure results in the host usually showing some overt signs and/or symptoms of the specific pathology or disease associated with that antigen. Another type of B lymphocyte, known as a memory B cell, is created as the primary immune response is terminated. Memory B cells carry the description of the antigen, so it will be recognized more quickly and acted against more rapidly the next time the antigen is encountered.

If the host survives the primary encounter with the antigen, a second exposure activates the memory B cells, which initiate an immediate, full immune response to the antigen. This is called the **secondary immune response. Memory cells** live for decades and are ready to mount an immediate antibody assault when triggered by a "remembered"

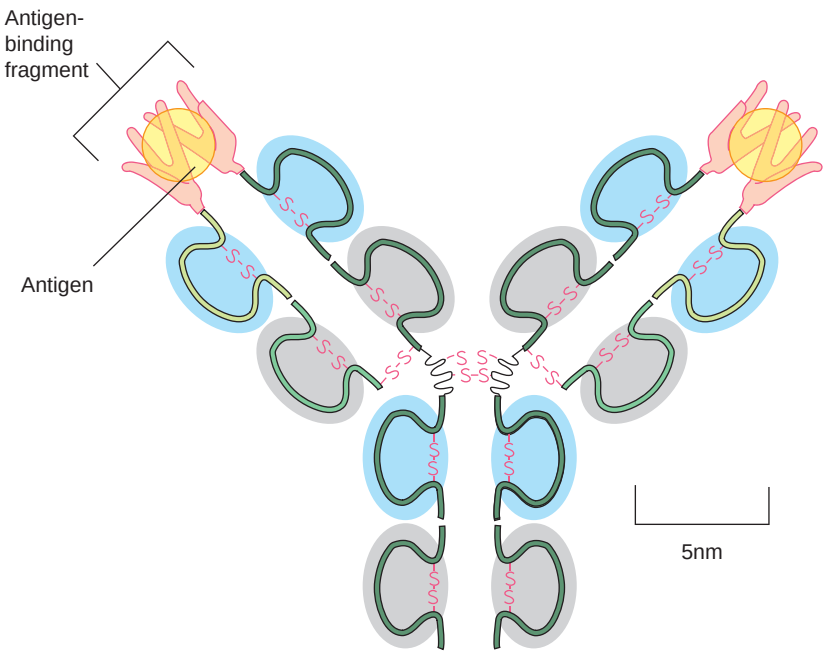

FIGURE 4.2. Antigen-binding fragment (Fab). The antigen-binding fragment is the area on the immunoglobulin that binds with an antigen.

BOX 4.1

Antibody Actions Against Antigens

1. Neutralize bacterial toxins
2. Bind with viruses to prevent entrance into cells
3. Cause the agglutination or clumping of antigens to facilitate phagocytosis
4. Bind to the surfaces of the antigen to aid in phagocytosis (opsonization)
5. Bind with an antigen to activate the complement system

antigen. The various ways in which antibodies attack circulating antigens such as bacteria, viruses, and toxic substances are listed in Box 4.1.

Antibodies. There are five major groups of antibodies or **immunoglobulins (Ig)** produced by the B lymphocytes. Figure 4.3 illustrates the molecular structure of these major groups.

1. IgG (four types): IgG (gamma globulin) is a circulating antibody and is directed against common infectious agents such as viruses, bacteria, and toxins. IgG binds to the antigen and then binds to a surface receptor on a phagocytic cell allowing for phagocytosis of the antigen–antibody complex. IgG also activates the classic pathway of the complement system and is active in the secondary immune response. IgG is the only immunoglobulin that crosses the placental barrier and protects the developing child and newborn until his or her own immune system matures. IgG makes up 80% of the circulating antibodies in the adult body.
2. IgM: This antibody is found on the surface of B cells and is the largest of the immunoglobulins. It may have up to 10 antigen-binding fragments available for use. This is the first antibody that is produced in response to an antigen. Its main purpose is to cause clumping, or agglutination, of antigen proteins during the primary immune response. IgM is more efficient in activating the classic pathway of the complement system than any of the other immunoglobulins.
3. IgA (two types): IgA is found in secretions such as saliva, tears, and the mucus secretions of the respiratory, gastrointestinal, and genitourinary tracts. IgA is secreted by plasma cells located in the epithelium of these tissues/organs. These secretions form part of the primary defense mechanism of the body by preventing the attachment of the pathogens to epithelial cells. IgA can activate the alternative pathway of the complement system. In addition, IgA is found in breast milk and can help protect the newborn infant.
4. IgE: IgE is secreted by plasma cells in the skin and mucous membranes. IgE triggers the release of histamine from mast cells and basophils and is important in the inflammatory response. It is also the antibody responsible for the symptoms of immediate hypersensitivity (anaphylactic) allergic reactions. IgE helps to protect the body from some parasitic infections, such as intestinal worms. An antigenic substance on the surface of the worms stimulates the release of histamine from mast cells in the intestinal mucosa. Histamine increases the permeability of the intestinal lining causing a large amount of water to flow into the intestine causing diarrhea, which is meant to result in expulsion of the worms.
5. IgD: IgD is found on B lymphocyte cell surfaces and is necessary for proper B cell differentiation during the maturation process.

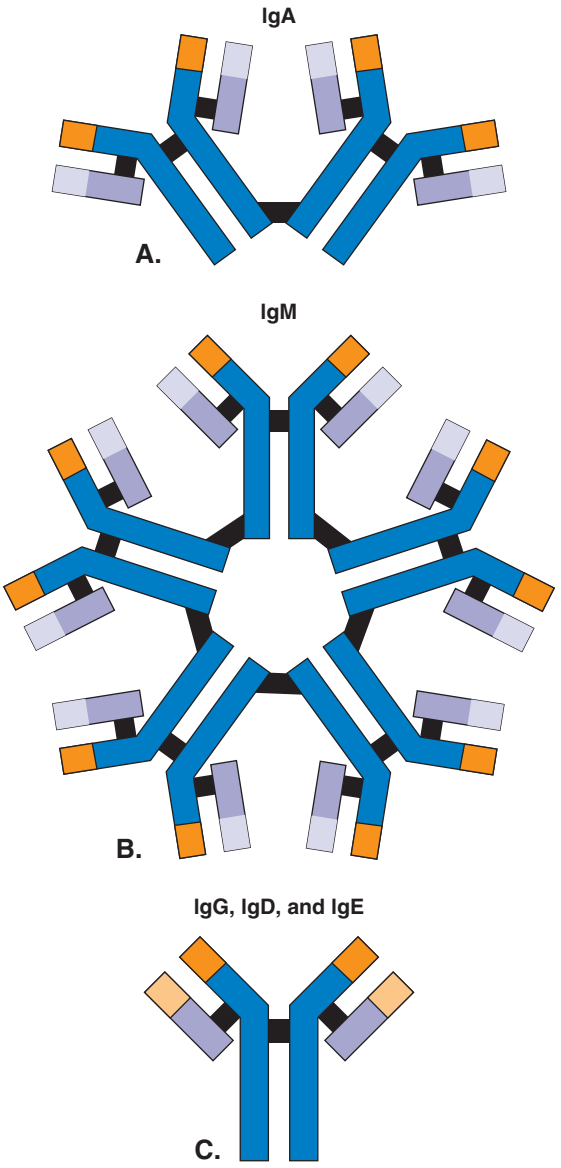

FIGURE 4.3. Molecular structure of immunoglobulins. The five major groups of immunoglobulin are represented by three different molecular structures. **A.** The molecular structure of IgA. **B.** The molecular structure of IgM. **C.** IgG, IgD, and IgE share the same type of structure.

The humoral response uses antibodies to neutralize extracellular pathogens and toxins. However, because antibodies work on the surface of cells, they cannot neutralize microbes residing and replicating within the cells. Cell-mediated immunity is primarily directed at destroying virus-infected cells but also plays a major role in destroying intracellular

parasites and bacteria. In addition, cell-mediated immunity is often able to destroy tumor/cancer cells and damaged host cells or those containing damaged DNA.

Cell-Mediated Immunity. Cell-mediated immunity is specific for host cells (**target cells**) that have become infected with viruses or have undergone change and are possible sources of harm for the individual. The end result of the cellular immune response is the destruction of the target cell. Cells involved in this response are always lymphocytes and include the following: T lymphocytes, natural killer (NK) cells, and macrophages.

T lymphocytes. T lymphocytes develop in the bone marrow from the same precursor or stem cells from which B lymphocytes develop. However, instead of maturing in lymphoid tissue, T lymphocytes mature (become self-tolerant) and differentiate (become antigen specific) in the thymus and are stored in lymphatic tissue throughout the body. T cells must be activated to function. Activation usually occurs when an **antigen-presenting cell (APC)** phagocytizes or otherwise binds to an antigen and brings it to the T cell. The most common APCs are macrophages, monocytes, and B cells. After the APC presents its antigen to the T cell, the T cell is activated against that antigen. Cytokines called interleukins assist in the activation of the T cells. The activation stimulates the T cell to divide and produce several types of T lymphocyte that are specific for the activating antigen. Some T cells can live for long periods of time and maintain their antigenic specificity, becoming T memory cells. The T cell functions are determined by protein molecules carried on their surfaces, which are called clusters of differentiation (CD). There are other types of cluster designations, but the following are the most significant:

1. $CD4^+$ or T helper cell: These cells regulate the action of all the other cells of the immune system. They increase or enable the functioning of B lymphocytes, macrophages, NK cells, and other T cells by the release of cytokines (see Table 4.1). Humans normally have twice as many $CD4^+$ cells circulating in the blood as $CD8^+$ cells.
2. $CD8^+$ or **T cytotoxic cell:** These cells are able to kill cells that have been recognized as being antigenic, such as cells infected with viruses, cancer cells, and sometimes normal cells the body has confused as nonself. The cytotoxic cell must be activated by a T helper cell or macrophage before it can bind to and destroy the antigen. The cytotoxic cells are active in tissue and organ rejection. In addition, some $CD8^+$ cells play a role in suppressing or stopping the immune response to a specific antigen.

Natural killer cells. **Natural killer (NK) cells** are similar to the cytotoxic T lymphocytes. The difference is they do not need to be sensitized to an antigen before reacting with that antigen. In other words, they have the ability to recognize foreign substances without any input from other cells or chemical mediators. These cells recognize and destroy virus-infected cells and other abnormal cells. NK cells can respond immediately to the presence of one of these cells and thus play a very important role in the immune system. Often NK cell functions are impaired in immune deficiency disorders such as acquired immunodeficiency syndrome (AIDS), where infectious agents and abnormal host cells normally controlled or eliminated by the immune system are allowed to remain and cause damage. There is also evidence NK and cytotoxic T cells play a part in detecting and eliminating cancer cells before they can multiply. More research is currently being conducted in this area.

Macrophages. As stated in Chapter 3, macrophages provide a crucial cellular link between the inflammatory process and the immune system response. Macrophages are monocytes that have left the circulating blood to enter connective or other tissues where they develop into macrophages. Histiocytes are macrophages found in connective tissue, Kupffer cells are macrophages found in the liver, and Langerhans cells are macrophages found in the epidermis (Fig. 4.4). These are all large, mononuclear, phagocytic cells that are considered part of cell-mediated immunity. They do not have to be sensitized by an antigen to recognize it and destroy it. Like polymorphonuclear neutrophils (PMN), macrophages have receptors on their surfaces that recognize opsonized matter. Unlike PMNs, macrophages can be activated to become even more destructive by chemical mediators released by $CD4^+$ T cells, for example, gamma interferon. Activated macrophages are able to secrete many more chemical mediators and have enhanced capabilities related to chemotaxis, phagocytosis, and antigen presentation. In addition, activated macrophages exhibit increased metabolism, size, and ability to adhere to, and spread on, surfaces. When this high level of destruction is no longer necessary, other chemical mediators are released that deactivate the macrophages. After the macrophage destroys the antigen, it will present specific proteins from the antigen to a T lymphocyte, thereby activating the lymphocyte and starting the immune response. Macrophages can survive for years, and because they retain no memory of an antigen after it has been destroyed, they must be reactivated when they encounter the same antigen

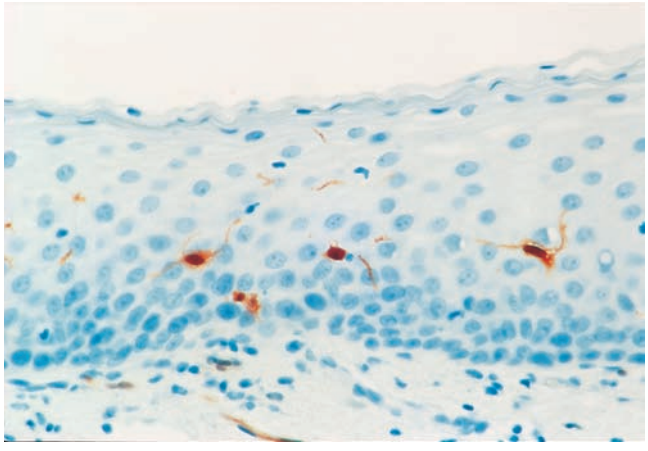

FIGURE 4.4. Langerhans cells. Langerhans cells (stained *brown*) can be seen in a section of epidermis. These macrophages can extend their cytoplasm in the form of dendritic processes to help capture and hold onto antigenic agents. (Mills SE., Histology for pathologists. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 2007).

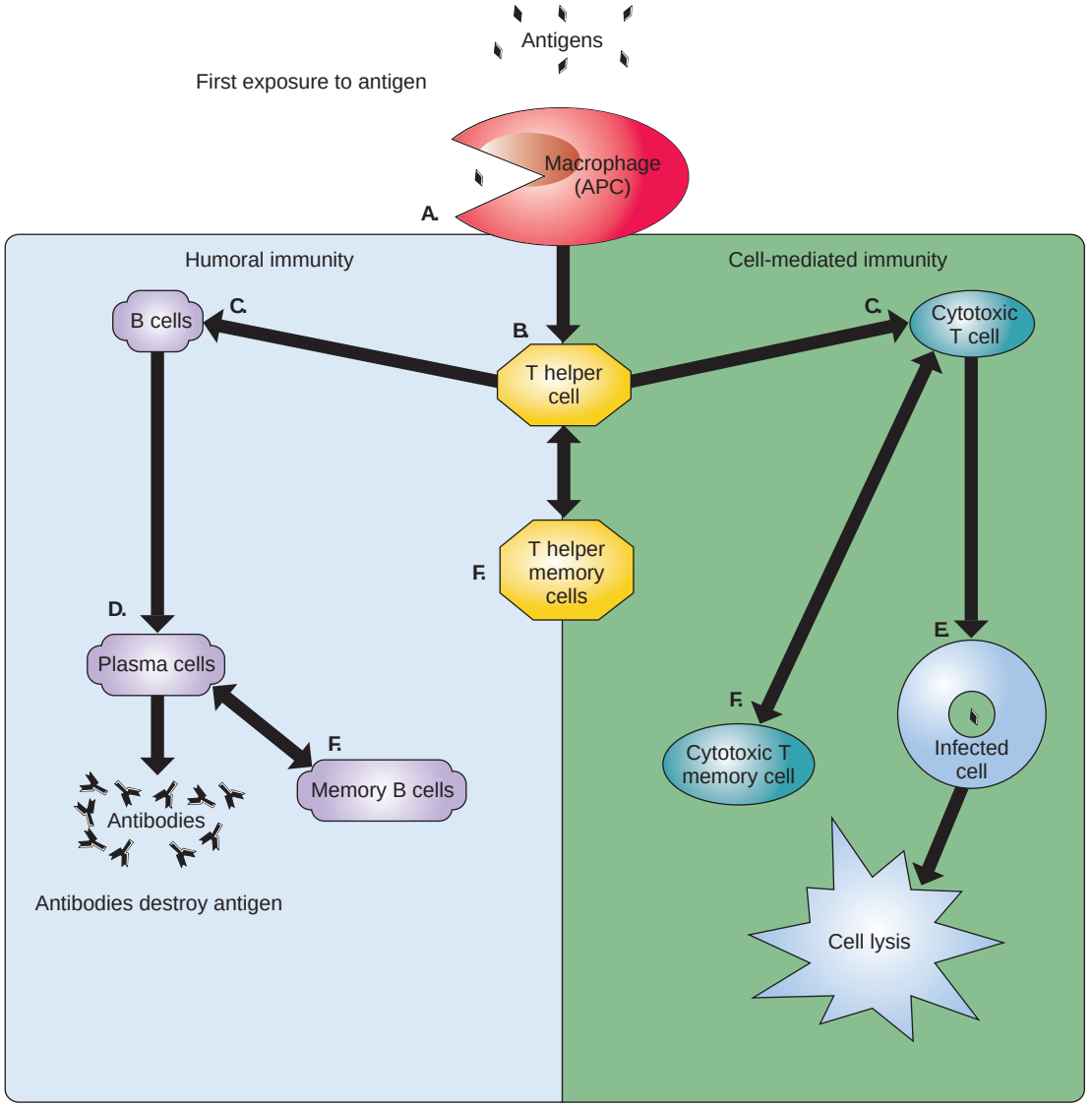

FIGURE 4.5. Humoral and cell-mediated immune responses and how they relate to each other. **A.** Initial exposure. The antigen is phagocytized by an antigen-presenting cell (APC), in this case, a macrophage. **B.** Antigen presentation. The macrophage or other APC presents the antigen to a T helper cell. **C.** T helper cell activates other lymphocytes. The T helper cell activates B cells and cytotoxic T cells. **D.** Plasma cell formation. Activated B cells produce plasma cells that begin to produce antibodies against the antigen. **E.** Cytotoxic T cell activation. Activated cytotoxic T cells attack cells that are infected with the antigen, causing cell lysis. **F.** Immunity established. T helper cells create T helper memory cells, plasma cells produce memory B cells, and cytotoxic T cells produce cytotoxic T memory cells. A second encounter with the antigen (not pictured) stimulates the T helper memory cells to activate cytotoxic T memory cells that will cause infected cells to lyse and B memory cells that will begin to produce antibodies specific for the antigen.

again. The nonspecific nature of the macrophage assists in helping the immune system respond immediately to injurious agents. The cell-mediated immune response results in destruction of the target cells and/or activation of the humoral immune response. Figure 4.5 illustrates the interrelationship between humoral and cell-mediated immunity and the importance of macrophages to both.

Types of Specific Immunity. The integrated efforts of the two components of the immune system enable the body to mount an immediate response to an antigen the next time it is encountered so the host is able to avoid any pathology the antigen would have caused. There are two forms of specific immunity: active and passive.

Active Immunity. **Active immunity** occurs when antibodies are produced by the body in response to an antigen. This can happen naturally, by an individual having an infectious disease, such as varicella-zoster virus (chicken pox), or it can occur through artificial means by vaccination. Vaccines contain either killed or attenuated (weakened) bacteria or virus or chemically altered toxins. Active immunity produces long-term immunity because memory cells created in response to the antigen will reproduce for the life of the host. Booster shots are often given just to make sure the memory stays strong and to strengthen the antibody response. Types of vaccinations include polio, tetanus, hepatitis A and B, measles, mumps, rubella, and so on.

APPLICATION **4.1**

How Vaccinations Work

Scenario 1: Mary is 5 years old and goes to day care at a neighbor's house with six other children. She has never been vaccinated for any childhood illnesses. Mary's friend Heather becomes sick with the measles. Mary has come in contact with the rubeola virus. How does the immune system respond?

1. Recognition
   a. B cell surface antibodies come in contact with the virus and bind to it.
   b. The B cell acts as an antigen-presenting cell and binds with a T cell.
   c. The B cell and the T cell are now activated against the rubeola virus.
2. Reaction
   a. The activated B cell produces both plasma cells that secrete antibody specific for rubeola and memory cells that will carry the image of the antigen for future encounters.
   b. The activated T cell produces $CD4^+$ helper cells and $CD8^+$ cytotoxic cells. Using cytokines, the helper cells will enhance the functioning of the B cells and call the macrophages and natural killer cells into action. The cytotoxic cells will begin to destroy any of Mary's cells that have become infected by the virus. The reaction time is slow during this initial encounter with the virus, and 10 to 12 days after Mary came in contact with the virus she begins to show symptoms of fever, upper respiratory congestion, cough, and general malaise. Mary breaks out in a generalized **maculopapular** (erythematic, raised) rash about 2 days after the other symptoms appear. These symptoms are the result of a systemic inflammatory response that has been initiated as a result of both the immune response and activation of the complement system. Four to seven days later, the symptoms begin to dissipate, and Mary feels much better. Her immune system will remember this encounter.
3. Remember
   a. Mary's immune system has produced both B memory cells and T memory cells that will react faster and to a much higher degree the next time they encounter the rubeola virus. During subsequent exposures, the secondary immune response will stop the virus before it can produce any manifestations of the disease.

Scenario 2: Once again, Mary is 5 years old and goes to day care at a neighbor's house with six other children. However, this time she has been vaccinated for all appropriate childhood illnesses. Mary's friend Heather becomes sick with the measles. Mary has come in contact with the rubeola virus. How does the immune system respond in this situation?

1. Recognition
   a. Mary received her vaccination for measles when she was supposed to.
   b. The vaccination stimulated Mary's immune system to produce B and T cells, including memory cells, which were activated against the rubeola virus.
   c. B and T memory cells come in contact with the rubeola virus at this time, and they know exactly what to do.
2. Reaction
   a. The activated B memory cells initiate the production of enormous amounts of both plasma cells that secrete antibody specific for rubeola and memory cells that will carry the image of the antigen for future encounters.
   b. The activated T memory cells produce $CD4^+$ helper cells and $CD8^+$ cytotoxic cells. Using cytokines, the helper cells will enhance the functioning of the B cells and call the macrophages and natural killer cells into action. The cytotoxic cells will begin to destroy cells that have become infected by the virus, if any. Mary never shows any signs that she has come into contact with this disease. Even though this is the first time she has encountered the viable virus, her immune system was ready for it and treated it as a second encounter. Her vaccine-primed immune system has done its job.
3. Remember
   a. Mary's immune system still has the memory cells, now primed and ready for a third encounter.

Passive Immunity. **Passive immunity** occurs when the host does not form his or her own antibodies but is given antibodies derived from another source, either human or animal. This type of immunity is short-lived because there is no memory produced in the individual's own immune system. There are no B cells activated by antigens to produce plasma or memory cells; in other words, the individual is still subject to infection. Passive immunity occurs naturally prior to birth when maternal antibodies are transferred across the placenta to the infant. It occurs artificially when an individual is given an injection of specific antibodies from a second source, very often a horse. The immunoglobulin used most often for this purpose is gamma globulin (IgG). For example, gamma globulin is given to unvaccinated dental health care workers who have a needlestick injury or percutaneous (through unbroken skin) exposure to the hepatitis B virus, as a form of postexposure prophylaxis to try to boost the immune response against any viral particles that may have entered the body.

Immunopathology

The previous information depicts how the immune system is supposed to function. Many times, the immune system does not function the way it should. The problems resulting from dysfunction of the immune system can be grouped into three major categories: hypersensitivity reactions, autoimmune diseases, and immune deficiency diseases.

Hypersensitivity Reactions

Hypersensitivity reactions set the immune system against the host and in many cases become destructive to the individual. Imagine a person who does not like peanut butter. That person will avoid contact with the offending food as much as possible. This is a conscious decision the individual makes, and if peanut butter is eaten, nothing results but a bad taste. The cells of the body cannot make this type of conscious decision. Their decisions are preprogrammed by either environmental or genetic factors. Hypersensitivity reactions occur when the body's cells come into contact with something they dislike or think will harm them in some way. In many cases the offending agent or antigen, for example peanut butter, is not harmful to a majority of the general population. In other cases, the antigen may even be part of the individual's normal cellular makeup. Statistics show the number of individuals who are hypersensitive to one or more substances is rising dramatically. One theory proposed in the late 1980s is starting to gain support as the results of numerous epidemiological studies are reported. This theory states that the environment in industrialized countries is becoming too clean and children are being exposed to too few microorganisms, fungi, and other examples of "dirt." A decrease in the number of exposures to these microbes and substances in childhood appears to be related to an increase in the incidence of asthma and other allergic reactions. Application 4.2 explores this theory in more detail.

Four types of hypersensitivity reactions may occur in response to an antigen. The first three types are immediate responses and are mediated or controlled by antibodies; the last type is a delayed reaction and is mediated or controlled by a cellular response. Remember, most of these reactions are self-limiting. When the agent causing them is gone, the reaction will stop.

Type I (Anaphylactic or Atopic Reactions)

Type I hypersensitivity reactions occur immediately (within minutes) after exposure to a previously encountered antigen such as penicillin, cat hair, or pollen. These antigens are usually not harmful to the general population, only to specific individuals. This reaction has two major forms: systemic or **anaphylactic reactions** and **atopic reactions** that include skin reactions, asthma, and upper respiratory manifestations. The systemic form causes the most dramatic reactions. These include hypersensitivity reactions

APPLICATION **4.2**

The Hygiene Hypothesis

The burden of infectious disease in industrialized societies has been steadily decreasing over the last five or six decades; meanwhile, the number of allergic and autoimmune disorders has been steadily increasing. In 1989, David P. Strachan proposed what is known as the "Hygiene Hypothesis" to explain why this might be occurring. The theory states that exposure to numerous types of bacteria, viruses, parasitic worms, and other toxins in early childhood helps instruct the immune system to develop immune tolerance. Without this "instruction," it is proposed the immune system may overreact with allergies or turn on itself with autoimmune disorders.

Research does not consistently support or refute the concept. Increasing family size, early attendance in childcare facilities or playgroups, growing up on a farm, and having pets all seem to be associated with a decreased risk of atopic disorders (allergic conditions). Some of the more interesting studies reviewed show a significant decrease in atopy in children who have grown up on farms and have consumed raw or unpasteurized milk. Studies investigating the types of microbes that may have a protective effect against allergy have reported that nonpathogenic or background microbes might play the dominant role. Other studies refute some of these findings asking questions, for example, why is the rate of asthma the same in affluent neighborhoods as it is in crowded, unhygienic, city slums?

Of interest, one study done by Rees Clayton et al. (2011) relates the use of Triclosan, a common ingredient in toothpaste, and other personal care and antimicrobial products, to the Hygiene Hypothesis. This study found more allergy diagnoses in subjects under the age of 18 who had higher urinary levels of Triclosan than those with lower concentrations of the chemical. The authors propose the higher concentrations showed more exposure to the antimicrobial and, one could reasonably deduce, less exposure to microbes needed to "instruct" the immune system.

Enhancing microbial exposure may have other positive effects as well. Several studies have shown decreases in C-reactive protein, a proinflammatory marker associated with the development of cardiovascular disease, in those individuals brought up with farm animals and who have had bouts of diarrhea during childhood. Clinical trials are being conducted in the United States and Europe using a particular species of "pig whipworm" as a treatment for peanut allergies, ulcerative colitis, Crohn disease, and multiple sclerosis (all associated with inappropriate immune system responses). They are also considering testing its use in the treatment of asthma. The whipworm is given orally, in egg form, and once established appears to inhibit the immune response (allergic reactions) in these individuals, lessening their symptoms.

Scientists are quick to remind us that this does not mean accepted infection control procedures and important personal hygiene measures such as frequent handwashing are not crucial. In fact, developing infectious disease in early life is associated with a slightly increased risk for asthma and atopic dermatitis. It is imperative we continue to protect ourselves against harmful organisms as everyday hygiene and sanitary measures have all played an essential role in decreasing the rate of illness and death from infectious disease we see today. Whether right or wrong, the Hygiene Hypothesis is giving the scientific community much to consider.

to bee stings, peanuts, and latex, which are life altering for those affected by them. Individuals who are allergic to these substances must be on constant alert so that they do not come into contact with them.

In the systemic form, plasma cells produce IgE in response to a particular antigen the first time it is encountered. The resulting IgE attaches to the surface of mast cells throughout the body. When the mast cells encounter that antigen again, they release granules containing histamine, which causes dilation and increased permeability of the blood vessels. As a result, blood pressure falls, and the entire circulatory system may shut down. Breathing is also impaired because histamine causes constriction of the smooth muscles in the bronchioles and tissue edema. This is a life-threatening emergency and must be recognized and treated quickly or the individual may die. Many individuals with known allergies wear medical identification tags to alert medical personnel about their allergy should they ever become unable to do so and need medical care. This is especially important if an individual is allergic to drugs or materials such as latex that would be used in a medical emergency.

The most effective treatment for an anaphylactic reaction is injected epinephrine. Epinephrine causes constriction of the dilated blood vessels, which increases blood pressure, and relaxation of the smooth muscles in the lungs, opening the airways. Individuals who may have severe anaphylactic reactions have access to this medication in the form of an EpiPen. The EpiPen carries a single dose of epinephrine that is easily injected by even young children. Other drugs used to treat anaphylactic reactions include oral antihistamines and corticosteroids. Box 4.2 describes the sequence of events in a type I anaphylactic hypersensitivity reaction.

The atopic form of type I reaction is exemplified by hay fever and mold and animal allergies. The symptoms associated with atopic type I reactions depend upon where the antigen comes into contact with the body. Hay fever (sneezing, sinus edema, and watery eyes) will become evident if contact is made in the upper respiratory system. Asthma may be the result if contact is made in the lungs, and diarrhea and vomiting may result if contact is made in the gastrointestinal tract. If the reaction is within the skin, a superficial swelling called hives or urticaria (Fig. 4.6) may manifest or a swelling of the deeper subcutaneous or submucosal tissues called **angioedema** (AE) may occur. Both conditions are usually IgE dependent and the result of an abrupt localized increase in vascular permeability caused by the release of histamine. In some instances, urticaria and/or AE may not be related to IgE or histamine. Nonallergic instances of AE may be associated with aspirin, nonsteroidal anti-inflammatory drugs (i.e., ibuprofen), ACE inhibitors, infection, trauma (i.e., heat or cold), and psychological stress, or the cause may be unknown. One form of AE, hereditary AE, is caused by a genetic defect that allows unchecked activation of the complement cascade causing prolonged vascular permeability (Frank, 2011). AE often involves swelling of the lips, tongue, and other oral and pharyngeal tissues (Fig. 4.7). Sometimes, the swelling is so severe there is a danger of airway obstruction,

FIGURE 4.6. Type I hypersensitivity reaction. This is an example of urticaria or hives seen with a type I hypersensitivity reaction. (From Goodheart HP. Goodheart's photoguide of common skin disorders. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

FIGURE 4.7. Angioedema (AE). AE is a diffuse, nonpitting, tense swelling of the dermis and the subcutaneous tissue. It develops rapidly and typically disappears over subsequent hours or days. Although usually allergic in nature and sometimes associated with hives, AE does not itch. (From Neville B, et al. Color atlas of clinical oral pathology. Philadelphia: Lea & Febiger, 1991, with permission.)

BOX **4.2**

Sequence of Events in a Systemic Type I Anaphylactic Hypersensitivity Reaction

1. Contact with allergen
2. Release of histamine from sensitized mast cells
3. Blood vessels dilate and exudate forms
4. Blood pressure falls
5. Venous return to the heart decreases
6. Cardiac output decreases
7. Circulation decreases
8. Circulatory system collapse

and emergency care must be obtained. AE may also affect other parts of the body such as the hands, feet, and the mucosa of the intestinal tract.

Localized reactions are usually treated with drugs that control or inhibit the release of histamine (antihistamines) or act on other elements of the immune response, such as the release of leukotrienes or cytokines. Severe localized reactions may also be treated with epinephrine.

NAME: Latex hypersensitivity

Etiology: Contact with natural rubber latex (NRL) proteins causes a type I latex hypersensitivity.

Method of Transmission: Inheritance may play a role in the development of allergies, and latex hypersensitivity is more common among individuals who have allergies to other substances. There is also an increased risk of developing a latex hypersensitivity with continued exposure to the protein.

Epidemiology: Latex hypersensitivity is estimated to occur in 1 to 5% of the general population. Data suggest that up to 17% of health care workers are latex sensitive (Behrman & Howarth, 2008). Other populations at higher risk for developing latex hypersensitivity include patients with spina bifida, urogenital abnormalities, and those who have had multiple surgeries. Individuals who are allergic to certain foods may also be allergic to latex because the molecular structure of the foods they are allergic to is very similar to the latex proteins. Box 4.3 lists foods that appear to have molecular structures similar to latex. There is equal distribution of this type of hypersensitivity among males and females.

Pathogenesis: Contact with the NRL proteins can occur through the skin or mucous membranes, or the proteins can be inhaled or injected. Exposure to the NRL proteins triggers an immediate type I anaphylactic reaction. When mast cells previously sensitized by IgE produced in response to an initial exposure to NRL come into contact with NRL proteins a second time, they release granules that contain histamine. Histamine causes the myriad of symptoms associated with the anaphylactic reaction.

Extraoral Characteristics: Symptoms are systemic, not localized, and generally appear within minutes of the exposure and include a generalized burning feeling in the skin or mucous membranes, pruritic rash or urticaria, runny nose, watery eyes, and sneezing. Symptoms seen in the most severely hypersensitive individuals may continue to worsen, causing asthma-like breathing difficulties, gastrointestinal cramping and diarrhea, hypotension, and eventual cardiovascular collapse and death.

Perioral and intraoral characteristics: Mucous membranes can become swollen, and the patient may experience burning sensations and/or pruritus. Laryngeal spasms can make speaking and swallowing difficult.

Distinguishing Characteristics: The abrupt immediate manifestation of the symptoms associated with anaphylaxis is somewhat distinguishing.

Significant Microscopic Features: Not applicable.

Dental Implications: Latex hypersensitivity has numerous dental implications for not only the patient but also the dental health care worker. Many items in the dental office may contain latex and could be the source of an exposure for a hypersensitive person. Box 4.4 lists common items found in a dental office that may contain latex. Examination gloves worn during dental treatment can be a source of exposure for both the patient and the dental health care worker. In fact, continued daily exposure to latex examination gloves increases the risk an individual will become sensitive to the NRL protein. In addition, powdered latex gloves can contaminate the air with powder containing molecules of NRL proteins. This powder can come to rest on any surface and be picked up by the skin when someone touches the surface, and it can be inhaled into the lungs. Glove manufacturers have developed low-protein latex gloves that may help to prevent sensitization to the NRL protein but will not eliminate or even minimize a hypersensitivity reaction. Many dental offices have established a latex-free glove policy and have attempted to replace patient care items containing latex with latex-free items. Box 4.5 lists recommendations for treating the latex-sensitive patient in

BOX 4.3

Food Allergies Associated with an Increased Risk of Latex Hypersensitivity

- Banana
- Kiwi
- Avocado
- Chestnut
- Peach
- Nectarine

BOX 4.4

Dental Office Items/Equipment That May Contain Latex

- Blood pressure cuffs
- Stethoscopes
- Examination gloves
- Syringes
- Face masks
- Oxygen/nitrous oxide delivery systems
- Handpiece and air/water syringe hoses
- Suction hoses
- Irrigation tubing
- Rubber dams
- Bite blocks
- Prophy cups
- Prophy angles
- Orthodontic elastics
- Protective eyewear
- Interdental stimulators

BOX 4.5

Recommendations for Treating Latex-Sensitive Patients in the Dental Office

- Schedule patient for the first appointment of the day
- Have no latex products in the treatment room
- Make sure instruments have not been handled with latex gloves
- Watch for powder from latex gloves on clothes and equipment
- Have a supply of latex-free supplies stored in a sealed container
- Have the medications and equipment necessary to treat a latex hypersensitivity reaction

the dental environment. Even if all precautions are taken, a latex-sensitive individual could possibly have a significant latex exposure during dental care. It is essential the dental professional investigate any possibility of a latex allergy indicated by the patient's health history.

Differential Diagnosis: A type I hypersensitivity reaction can be caused by almost any substance that comes in contact with a susceptible individual. Other conditions that might have similar symptoms include:

1. Asthma–Chapter 10. The sudden abrupt onset and breathing difficulties experienced during an asthma attack are similar to those seen in anaphylaxis.
2. Acute adrenal insufficiency–Chapter 7. Symptoms of vomiting, abdominal pain, hypotension, and cardiovascular collapse are similar to those seen in anaphylaxis. This condition can quickly lead to coma and death. Respiratory distress is not a significant feature of this condition; neither are urticaria or runny nose and watering eyes.
3. Hypoglycemia–Chapter 7. Hypoglycemia or insulin reaction could mimic some of the symptoms of an anaphylactic reaction, specifically, confusion and unconsciousness.

Treatment and Prognosis: Prevention is the best policy in cases of latex hypersensitivity, and the best way to prevent the reactions is to avoid contact with latex. Treatment depends on the severity of the symptoms and usually consists of an injection of epinephrine followed by oral antihistamines. However, care must be taken because occasionally the patient will have a biphasic reaction. A biphasic reaction occurs several hours after the initial hypersensitivity reaction and must be treated with additional injections of epinephrine. This patient should be released into the care of emergency medical services (EMS). Most patients will recover from anaphylactic reactions with no ill effects; however, if treatment is not rendered immediately, these reactions can be fatal.

Type II (Cytotoxic Reactions)

Cytotoxic reactions occur when an antibody, usually IgG or IgM, combines with an antigen bound to the surface of specific cells in the host's body. In most cases, the reason an antigen is bound to the surfaces of these cells is unknown. The combination of the antibody with the antigen on the cell's surface can produce several results:

1. Trigger direct lysis or destruction of the affected cells
2. Cause the affected cells to malfunction in some way
3. Prepare the affected cells for phagocytosis by immune system cells

The classic example of direct lysis is the transfusion reaction that occurs when an individual is given an incompatible blood type. Another example of this type of reaction occurs in erythroblastosis fetalis. In this disorder, the mother is Rh^- and the fetus is Rh^+. Erythroblastosis fetalis occurs during a second pregnancy with an Rh^+ fetus, since it takes an initial sensitizing exposure or first pregnancy with an Rh^+ fetus to enable the hypersensitivity reaction. Maternal antibodies against the positive factor cross the placental barrier and destroy the red blood cells of the fetus, necessitating an immediate blood transfusion when the infant is born. This can be avoided if the at-risk mother is identified before the birth of the first child and is given injections of gamma globulin containing Rh antibody. The Rh antibody will prevent the sensitization of the mother and thus prevent problems with a future pregnancy.

Hyperthyroidism, as seen in Graves disease (see Chapter 7), is an example of a cytotoxic reaction in which the cells remain viable but malfunction and cause excess production of the thyroid hormones. Other forms of cytotoxic reactions occur when something happens that changes the MHC attached to some of the body's cells. The result is that the immune system thinks the affected cells are foreign and attacks them. This can also happen in the reverse. A problem in the immune system may cause it to get confused and attack cells that have had no alterations of their MHCs. The event that alters the cells or the immune system is very often unknown, or it may be related to a drug or environmental agent. If the problem is related to a drug or known environmental agent, removal of the offending agent should stop the hypersensitivity reaction and the resulting tissue damage. If the cause is unknown, the problem is considered an autoimmune dysfunction. Autoimmunity is discussed later in this chapter. Examples of autoimmune disorders considered to be type II hypersensitivity reactions are pemphigus vulgaris (see Chapter 11), cicatricial pemphigoid (see Chapter 11), and acute rheumatic fever (see Chapter 8).

Type III (Immune Complex-Mediated Reactions)

In **immune complex-mediated reactions** IgM, IgA, or IgG form antigen–antibody complexes with circulating antigens. The antigens can be exogenous, such as bacteria, viruses, drugs, or chemicals; or they can be endogenous, created by the body as part of an immune dysfunction. The damage to tissues is done when these antigen–antibody complexes are deposited in a particular part of the body and cause the initiation of the inflammatory response. Chemotactic agents released in the inflammatory response

FIGURE 4.8. Allergic contact dermatitis. This patient was hypersensitive to nickel and formed a pruritic rash under a watch that contained nickel. (Stedman's medical dictionary for the health professions and nursing. 7th ed. Baltimore: Lippincott Williams & Wilkins, 2011.)

cause PMNs to travel to the site or sites and release their destructive enzymes. These enzymes cause either local or systemic tissue destruction. Autoimmune examples of this type of reaction include systemic lupus erythematosus (see Chapter 12), rheumatoid arthritis (see Chapter 10), and forms of glomerulonephritis (kidney disease).

Type IV (Cell-Mediated or Delayed Hypersensitivity Reactions)

Cell-mediated reactions do not require the action of antibodies; instead, they involve specific T cells that have been sensitized to a particular antigen. The reaction either causes death of the involved cells or initiation of an inflammatory response. Type IV reactions are usually delayed and can take 24 to 72 hours or more for the full response to be observed. There are several forms of type IV hypersensitivity reaction: contact dermatitis, graft rejection, and autoimmune dysfunction.

Allergic contact dermatitis (ACD) is one of the most common forms of type IV hypersensitivity (Fig. 4.8). Haptens, very small antigenic molecules, such as oil from poison ivy and sumac leaves and certain chemicals in rubber, combine with skin proteins. The hapten–protein combination is captured by macrophages (APC) in the epidermis known as Langerhans cells that present the antigen to T cells. The T lymphocytes activate more macrophages and cytotoxic T cells that start destroying cells that have had contact with the allergen. The hypersensitivity reaction will not stop until the antigen is eliminated or the skin is destroyed. The most typical presentation involves the development of an extremely pruritic or itchy erythematic vesicular rash. The rash will continue to develop as all areas touched by the allergen (antigen) are involved (Fig. 4.9). Resolution can take several days or several weeks, depending on the antigen and the duration of the exposure. Prior exposure to the antigen is necessary as a sensitizing event, and the reaction is confined to the areas contacted. The same type of reaction occurs in the mouth. It is called contact stomatitis and has a variety of possible presentations including diffuse erythema, ulcers, and vesicles. Contact stomatitis is discussed further in Chapter 12. Examples of substances that can cause a contact allergic reaction are poison ivy, metals, cosmetics, and various chemicals, including those used in toothpaste and mouth rinse. Topical corticosteroids and anti-itch creams can help alleviate the symptoms associated with cutaneous rashes. Occasionally, systemic corticosteroids are used to treat severe reactions.

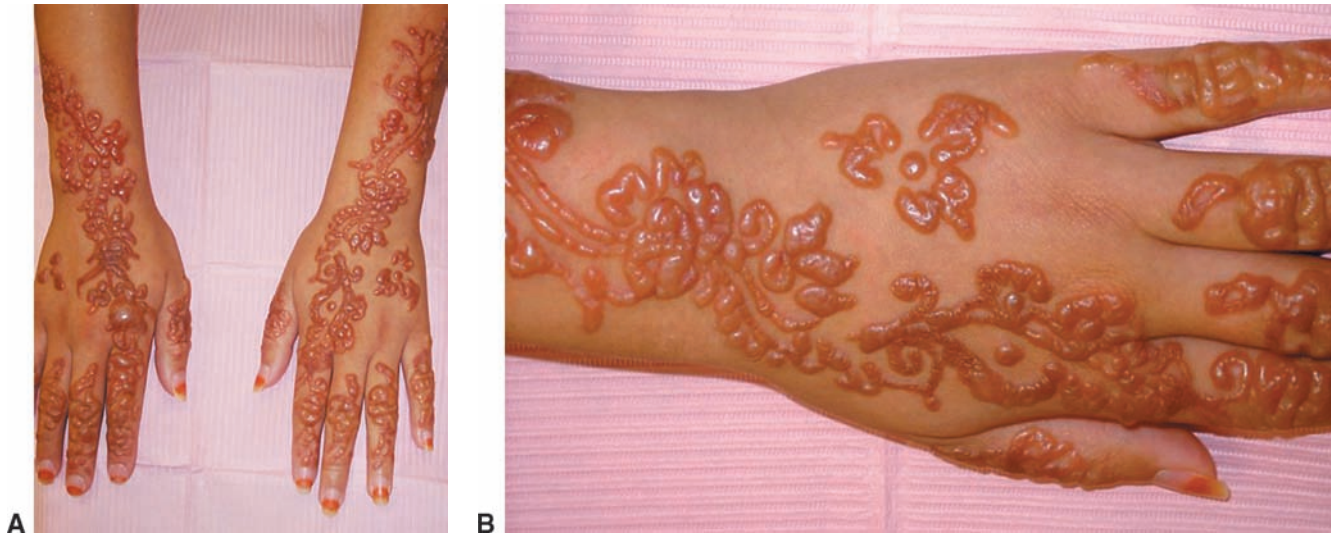

FIGURE 4.9. Allergic contact dermatitis from a henna tattoo. This is a dramatic example of the sharp line of demarcation between areas of contact with an antigen and those not touched as the vesicular rash clearly follows the pattern drawn with the henna. (Copyright of the New England Journal of Medicine: Evans CC, Fleming JD. Images in clinical medicine. N Engl J Med 2008;359:627–627.)

Tissue and organ graft rejection as seen in **graft-versus-host** or **host-versus-graft reaction** results from an immune response to MHC present on the surface of cells in the donor or recipient tissue. No matter how closely the MHCs are matched, they will not be identical (except in identical twins), and patients must take immunosuppressant drugs for the rest of their lives to control this reaction.

Current research supports evidence that Sjögren syndrome is an autoimmune type IV hypersensitivity reaction that results in salivary and other exocrine gland damage caused directly by T and B lymphocytes (see Chapter 17).

Allergic Contact Dermatitis Associated with the Use of Latex Gloves. ACD is more common than type I latex hypersensitivity reactions. ACD is caused by contact with the residue of chemicals used in manufacturing latex gloves. It is thought to affect about 5 to 20% of dental health care workers (DePaola, 2004). This delayed reaction occurs 24 to 48 hours after exposure of a sensitized individual to these substances. The skin becomes dry and cracked with repeated exposure (Fig. 4.10). ACD can be prevented by avoiding the use of latex gloves and by avoiding contact with other latex-containing items. Dental patients who indicate they have a latex allergy may have this type of reaction instead of the type I hypersensitivity reaction. Questions about the clinical signs and symptoms associated with their allergy should be all that is required to determine the type of reaction they have. Remember, latex allergy symptoms are not localized, so if the patient reports a localized skin reaction it is most likely ACD and not a type 1 latex allergy. If there is any doubt, the patient should be referred to a physician for definitive diagnosis.

Irritant Contact Dermatitis. **Irritant contact dermatitis** (ICD) is not a hypersensitivity reaction. ICD is a skin inflammation caused by exposure to caustic chemicals or mechanical irritation of the skin (Fig. 4.11). Many chemicals found in a dental office should only be used when hands are protected by gloves, for example, disinfectants such as glutaraldehyde and bleach. Mechanical irritation can be caused by gloves rubbing against the skin or by powder placed in some gloves to make them easier to put on. The symptoms of ICD are similar to those of ACD except for vesicle formation, making it difficult to differentiate between the two. Changing from latex to latex-free gloves, changing hand soaps, or making sure one does not directly contact disinfectants or other caustic chemicals may help to determine what type of dermatitis is present.

FIGURE 4.10. Allergic contact dermatitis (ACD). ACD associated with chemicals used in manufacturing latex gloves. (From Goodheart HP. Goodheart's photoguide of common skin disorders. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

FIGURE 4.11. Irritant contact dermatitis (ICD). This is an example of ICD in a health care worker who did not use appropriate protection while using chemical disinfectants. (From Stedman's medical dictionary for the health professions and nursing. 7th ed. Baltimore: Lippincott Williams & Wilkins, 2011.)

Autoimmune Diseases

As discussed above, the immune system usually functions under the premise of self-tolerance. When the immune system loses the ability to distinguish self from nonself or there is an alteration of the host's cells that changes their makeup (such as a change in an MHC), the immune system will attack the cells of the host just as if they were foreign matter, and an **autoimmune disease** becomes manifest. Most autoimmune diseases present or manifest as type II, III, or IV hypersensitivity reactions. The tissue damage done in these diseases is the direct result of the actions of the host's own immune and inflammatory responses. The damage may be throughout the body, as in systemic lupus erythematosus (see Chapter 12), or it may occur in a single organ, as in hyperthyroidism (see Chapter 7). Autoimmune diseases are usually chronic conditions that manifest with many exacerbations and remissions over many years. Many of the autoimmune disorders have a genetic predisposition for their occurrence. Table 4.2 lists common autoimmune disorders and the chapters in which they are discussed, based on the clinical appearance of their characteristic oral lesions. The dental hygienist may be the first health care

TABLE 4.2 **Chapter Locations for Immune System Disorders with Oral Manifestations**

Immune System Disorder	Clinical Appearance of the Characteristic Oral Lesions	Chapter Location
Cicatricial pemphigoid	Vesicles	Chapter 11, "Lesions that have a Vesicular Appearance"
Pemphigus vulgaris	Vesicles	
Bullous pemphigoid	Bulla	
Aphthous ulcers	Mucosal ulcers	Chapter 12, "Ulcers and Ulcer-like Lesions"
Systemic lupus erythematosus and discoid lupus erythematosus	Mucosal ulcers	
Behçet syndrome	Mucosal ulcers	
Reiter syndrome	Mucosal ulcers	
Erythema multiforme	Mucosal ulcers	
Lichen planus	White lesions	Chapter 14, "White Lesions"
Sjögren syndrome	Enlarged salivary glands	Chapter 17, "Soft Tissue Enlargements"
Salivary lymphoepithelial lesion	Enlarged salivary glands	
HIV infection and AIDS	Various	Chapter 22, "HIV and AIDS"

professional to observe signs of some of the autoimmune diseases such as pemphigus vulgaris, cicatricial pemphigoid, oral lichen planus, and systemic lupus erythematosus, all of which may present with oral lesions prior to any cutaneous lesions (Fig. 4.12).

Immune Deficiency Diseases

Hypersensitivity reactions and autoimmune disorders are examples of conditions that have their basis in an immune system that is overstepping its boundaries. Immune deficiency disorders occur when the immune system or part of it fails to function. Immunodeficiency diseases fall into two basic categories: primary (congenital) and secondary (acquired).

FIGURE 4.12. Systemic lupus erythematosus. The dental professional may be the first to observe the manifestations of some autoimmune disorders because they may present in the oral cavity prior to any cutaneous manifestations. Ulceration is present on the hard palate in this individual with systemic lupus erythematosus. (From Goodheart HP. Goodheart's photoguide of common skin disorders. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

Primary Immunodeficiency Disease

Primary immunodeficiency diseases are always caused by a genetic or congenital abnormality. "Congenital" is defined as existing at the time of birth. Congenital abnormalities are not necessarily caused by an inherited trait but may result from a spontaneous genetic mutation or a random developmental defect. The abnormality results in defective functioning of at least one part of the individual's immune system or inflammatory process. The problem may be that T cells do not function correctly or perhaps the complement system is dysfunctional because a specific protein is not created correctly. In either case, the result is an impaired ability of the host to fight off infection and maintain the health status of the body. There are numerous examples of primary deficiencies; this chapter examines selective immunoglobulin A deficiency (SIgAD) because it is the most common of the primary deficiency diseases, affecting approximately 250,000 people in the United States (Dolina & Bascom, 2011) and DiGeorge syndrome (chromosome 22q11.2 deletion syndrome) because of the possible perioral abnormalities that may result from this deficiency.

Individuals with SIgAD have B lymphocytes that are unable to produce IgA but are able to produce normal levels of IgG and IgM. These individuals are very often asymptomatic. They occasionally present with respiratory or gastrointestinal infections and they have a strong predilection for allergies, autoimmune diseases, and vascular disorders related to collagen structure and function. This condition may result in chronic sinus pain due to recurrent

upper respiratory infections and deafness due to numerous ear infections. Early diagnosis of SIgAD is important, as is aggressive prevention and treatment of infections.

DiGeorge syndrome is a genetic disorder that can be inherited or can result from a spontaneous genetic mutation occurring in the developing fetus. The problems associated with DiGeorge syndrome are caused by failure of the third and fourth pharyngeal pouches to develop. The thymus, parathyroid glands, and some of the thyroid gland are partially or totally missing. In addition, there may be errors in the formation of the face, ears, and mouth. Perioral abnormalities usually become more obvious as the individual ages and include retro or micrognathia, long face, high broad nasal bridge, cleft palate and/or lip, and microdontia. Those with this syndrome frequently have congenital heart defects and may also be developmentally delayed or have learning disabilities (Bawle, 2010). DiGeorge syndrome affects the T cells and B cells. The T cell level is diminished or altogether absent, making the individual more susceptible to viral and fungal infections. B cell activity, including the production of antibodies, is also diminished because B cells must be activated with the help of $CD4^+$ T helper cells. It is important for the dental hygienist to remember in all instances of immune deficiency that normal standard precautions for preventing the transmission of disease may not be effective, and any contact with a pathogenic organism may cause a fatal infection.

Secondary Immunodeficiency Disease

Acquired or **secondary immunodeficiency** diseases develop after birth and are not directly related to genetics. Any of the following conditions can be associated with an acquired immune deficiency: renal disease, cancer, malnutrition, diabetes, immunosuppressive drugs (corticosteroids) or treatments (radiation), advanced age, tuberculosis, HIV infection, and more. One of the most common causes of immune suppression is the use of corticosteroid drug therapy to control the myriad of inflammatory diseases found today. Corticosteroids depress the inflammatory response, thereby reducing the damage and symptoms associated with diseases such as rheumatoid arthritis and systemic lupus erythematosus.

Immune deficiency conditions allow **opportunistic infections** to overwhelm the host. Opportunistic infections are caused by organisms that usually pose no threat to the individual with a normal immune system. For example, individuals undergoing chemotherapy for cancer are at a high risk for overgrowth of oral *Candida albicans* (fungus) because their immune systems are not able to control this normally innocuous microorganism that lives with us in a commensal (causing neither harm nor benefit) relationship. The compromised individual is also at risk of having infections, such as periodontal disease, become more aggressive and severe than they would be in an individual with a normal immune system. The most prominent immune deficiency disease at this time is AIDS. Because of the number of oral and perioral manifestations of AIDS and the fact most of these are abnormal presentations of diseases discussed in later chapters, AIDS and HIV infection are presented in detail in Chapter 22.

SUMMARY

- Nonspecific immunity provides generic defenses to protect the body, including the first-line defense systems of the body such as the inflammatory response and the integumentary system.
- Specific immunity is designed to provide protection from specific threats to our health. The organs associated with specific immunity include the bone marrow, thymus, spleen, lymph nodes and vessels, and tissues scattered throughout the body.
- The immune response is directed against foreign substances or antigens that can be microbes, chemicals, donated organs or tissues, and sometimes the individual's own tissue cells.
- Lymphocytes and macrophages are the main cellular components of the immune system. The lymphocytes are further defined as B or T lymphocytes. B lymphocytes are active in humoral immunity, and T lymphocytes are more active in cell-mediated immunity.
- Cell-mediated immunity is specific for cells that have been infected or that the immune system sees as harmful. Cells active in cell-mediated immunity are the T lymphocytes, NK cells, and the macrophages.
- Macrophages or another APC phagocytize an antigen, process it, and present it to a $CD4^+$ T helper cell. With the aid of such cytokines as the interleukins, the T helper cell becomes activated against the antigen presented to it. The activated T cell can now enhance the actions of other immune cells against the antigen. It can activate B cells to produce plasma cells and $CD8^+$ cytotoxic T cells to actively search out and destroy the antigen.
- Humoral immunity involves the production of antigen-specific antibodies by B lymphocytes. The B lymphocyte encounters an antigen that can bind to its Fab. A cooperating $CD4^+$ T helper cell also binds with the B cell, and using cytokines in the form of interleukins, activates the B cell for the specific antigen bound to it. The end result is the creation of a plasma cell that produces antibody specific for that antigen. The plasma cell divides rapidly and produces more antigen-specific plasma cells that produce more and more antibodies. At the conclusion of this primary immune response, some B cells become memory cells so the antigen can be remembered and reacted to more quickly during a secondary immune response the next time the body encounters it.
- Active immunity is produced when the individual makes his or her own antibodies in response to an antigen. Active natural immunity occurs when an individual is exposed to the actual infection; active artificial immunity occurs when an individual is vaccinated with a live or attenuated antigen.

- Passive immunity occurs naturally as antibodies are transferred across the placenta and through breast milk to the infant and artificially when a patient receives an injection of immunoglobulins after exposure to an infection, for example, IgG after an exposure to hepatitis B virus.
- Hypersensitivity reactions are an abnormal immune response to an antigen that in most individuals is not harmful to the body. There are four types of hypersensitivity reaction: type I anaphylactic or atopic, type II cytotoxic, type III immune complex-mediated, and type IV delayed hypersensitivity reactions.
- Autoimmune diseases result when immune or self-tolerance fails. The immune system can cause direct lysis of the involved cells, initiate an inflammatory response to destroy the cells, or alter the functioning of the cells.
- Most autoimmune diseases are chronic and progressive and have remissions and exacerbations of the signs and symptoms many times over a period of years.
- Immunodeficiency diseases are either primary or acquired. Primary immunodeficiencies are present at birth but may not be caused by inherited traits. These disorders can affect the entire immune system or one or more parts of it.
- Acquired immunodeficiencies occur later in life and can be associated with chronic illness, malnutrition, diabetes, immunosuppressant drug therapy, and other systemic problems.

CHAPTER REVIEW

Case Study 4.1

Mehrnaz, a 19-year-old female, presents to your office for her 6-month "check-up." You review her medical history and discover no significant findings. Mehrnaz's dental history includes the loss of tooth #10 about 1 year ago during a gymnastic accident on the uneven bars. The lateral was replaced temporarily by a removable acrylic partial denture or "flipper" (Fig. 4.13). An extraoral examination yields no significant findings. You observe the condition depicted in Figure 4.14 when you perform your intraoral examination.

FIGURE 4.13. "Flipper" replacing tooth 10.

FIGURE 4.14. Erythema of the hard palate and the gingiva.

1. How will you describe Mehrnaz's hard palate and lingual attached gingiva?
2. What can you ask Mehrnaz about this area?
3. What do you think is causing the condition?
4. If this is a hypersensitivity reaction, which type of reaction is it? Why?

For answers and additional review activities, log in to **thePoint.lww.com**

Case Study 4.2

Jaime, an 18-year-old female, has been a patient in your office since she was a child. She and her family all have a history of allergic reactions to multiple foods and food additives, medications, and other substances such as cat and dog dander. You are taking her blood pressure when you notice the condition pictured in Figure 4.15 on her right arm.

1. Assuming this is a hypersensitivity reaction, what type is it?
2. What is the pathogenesis? List the steps in the reaction.
3. What questions will you want to ask Jaime?
4. Do you think you should proceed with treatment? Why or why not?
5. What type of emergency will you prepare for and how will you prepare for it if you decided to proceed with treatment?

FIGURE 4.15.

For answers and additional review activities, log in to **thePoint.lww.com**

Critical Thinking Activities

1. Why do some individuals come into contact with a disease and remain disease free, while others have the same contact with the disease and become ill with it?
2. Explain this statement. "People don't die from immunodeficiency diseases; they always die from some other condition."
3. What is your opinion of the "Hygiene Theory"? If the hypothesis is correct, what might the impact on everyday life be? Would you see a change in infection control practices within the dental office? Why or why not?

Portfolio Possibilities

- Choose an immune system disease associated with oral lesions and research the topic on the Web. Write a patient fact sheet describing the disease in lay terms and presenting possible oral manifestations of the disease. Discuss what patients might do to alleviate the oral signs of the disease and what products are available to assist them.
- Choose a disease associated with the immune system. Using current research and evidence-based resources, write a chairside reference sheet for your own use that includes a description of typical oral and perioral lesions, systemic manifestations, and health history clues that would alert you to the possibility of this condition. Discuss the implications of the disease for the dental professional, including any treatment modifications or consultations that might be necessary. Make a list of drugs available to treat the disease and their possible side effects, including dental side effects.

Media Menu

Web Sites

EnCognitive.com: Very visual explanation of how the immune system works; has PDF files of brochures and articles
http://www.encognitive.com/node/1114

KidsHealth: Nice site for obtaining health information for various levels of maturity. Teacher guides for preschool, teens and between
http://kidshealth.org

The Official Web Site of the Nobel Prize: Interesting information on the immune system; includes a game that works through the major functions of the system and other games relating to other body functions/organs
http://nobelprize.org/educational/

Multimedia Resource

Immune System - Natural Killer Cell video
http://youtu.be/HNP1EAYLhOs

Study Tools

Take advantage of additional online resources to help you study and ace your exams!

- Answers to case studies in the book
- Additional case studies and answers
- Interactive quiz bank with answer feedback
- Fully searchable e-book for quick lookup and studying on-the-go
- Printable Lesion/Condition Summary Table
- Expanded Media Menu with direct links to related Web sites and multimedia resources
- Supplemental references

thePoint Online resources and links are available at http://thepoint.lww.com/DeLong2e.

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Chapter 4 **LESION/CONDITION SUMMARY TABLE**

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Type I (Anaphylactic or Systemic) Reaction	Contact with a previously encountered antigenic substance	Contact with an antigen causes mast cells to release massive amounts of histamine resulting in hypotension, impaired breathing, and tissue edema; if untreated may result in circulatory system collapse and death	Initial symptoms may involve a burning feeling in skin or mucous membranes or urticaria, runny nose, watery eyes, and sneezing; as the reaction progresses, breathing becomes difficult and may have abdominal cramping, diarrhea, eventual unconsciousness, and death if not treated.	Not applicable	Treatment is given according to the severity of symptoms and past history of reactions. Call emergency medical services (EMS) for severe or unknown reactions. Injection with epinephrine followed by oral antihistamines is common; do not leave the patient unattended in case there is a biphasic reaction.	Prevention is the best treatment; obtain a complete medical/drug/dental history from each patient and update at every encounter. Have epinephrine and antihistamines available in the emergency kit.
Type I (Atopic or Localized) Reaction	Contact with a previously encountered antigenic substance	Same pathogenesis as above but on a localized level. The release of histamine occurs in a limited area or type of tissue depending on where the contact with the antigen occurs.	If contact is made in the upper respiratory system, symptoms are sneezing, edema, watery eyes; lungs—asthma; gastrointestinal (GI) tract—cramping, diarrhea; skin—urticaria; oral mucous membranes—angioedema, etc. Examples of atopy include hay fever, mold and animal allergies.	Not applicable	Treatment usually consists of oral antihistamines, or drugs that inhibit the production of leukotrienes of cytokines. Epinephrine may be used in some cases. The individual should avoid contact with the offending substances.	Prevention is the best treatment; obtain a complete medical/drug/dental history from each patient and update at every encounter. Have epinephrine and antihistamines available in the emergency kit.
Latex Hypersensitivity	Natural rubber latex proteins	Contact with natural rubber latex proteins occurs through skin or mucous membranes	Symptoms are systemic, appearing within minutes. Initial symptoms may involve a burning feeling in skin or mucous membranes or urticaria, runny nose, watery eyes, and sneezing; as the reaction progresses, breathing becomes difficult and may have abdominal cramping, diarrhea, eventual unconsciousness, and death if not treated.	Not applicable	Treatment is given according to severity of symptoms and past history of reactions. Call EMS for severe or unknown reactions. Injection with epinephrine followed by oral antihistamines is common; do not leave the patient unattended in case there is a biphasic reaction.	Prevention is the best treatment; obtain a complete medical/drug/dental history from each patient and update at every encounter. Endeavor to have a "latex free" office environment. Have epinephrine and antihistamines available in the emergency kit. Dental professionals should not routinely use latex gloves for any reason due to the risk of developing an allergy as a result of frequent latex exposures.
Type II (Cytotoxic) Reaction	Incompatible blood transfusion, erythroblastosis fetalis, autoimmune dysfunction	Antibody (IgG, IgM) combines with an antigen found on erythroblastosis fetalis, the surface of host cells resulting in (a) destruction (lysis) of the affected cell, (b) cell malfunction, and/or (c) phagocytosis of the cell.	Symptoms vary with the type of reaction; for example, hyperthyroidism seen in Graves disease and the heart valve destruction seen in acute rheumatic fever.	Not applicable	Treatment is different for each specific disorder and may include immunosuppressive drugs and other drugs that modify or inhibit specific elements of the immune system.	It is essential to obtain a complete medical/drug/dental history from each patient and update at every encounter to be aware of the presence of these disorders and research the specific disorder to make sure nothing is done to exacerbate symptoms or influence the course of the disease.
Type III (Immune Complex-Mediated) Reaction	Various antigenic agents (bacteria, viruses, drugs, chemicals); autoimmune dysfunction	Antigen–antibody complexes form with circulating antigens and are deposited in a specific part of the body, causing local or systemic tissue destruction.	Symptoms vary according to the specific disorder; for example, the damage to the joints in rheumatoid arthritis is caused by inflammation triggered by the deposition of the antigen–antibody complexes within the joints of the body.	Not applicable	Treatment for the disorders caused by this type of immune system dysfunction varies but usually consists of immunosuppressive drugs and other chemotherapeutic agents directed toward limiting the damage done by the deposited antibody–antigen complexes.	It is essential to obtain a complete medical/drug/dental history from each patient and update at every encounter to be aware of the presence of these disorders and research the specific disorder to make sure nothing is done to exacerbate symptoms or influence the course of the disease.

continues

Chapter 4 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Type IV (Cell-Mediated or Delayed) Reaction	Contact with previously encountered antigens	T cells become sensitized to a particular antigen resulting in death (apoptosis) of the affected cells or the initiation of the inflammatory response.	Cutaneous: Erythematic, pruritic, vesicular rash which takes days to weeks to resolve once the allergen is removed Intraoral: Allergic stomatitis (see Chapter 12)	Not applicable	Elimination of allergen, topical corticosteroids, anti-itch creams; systemic corticosteroids may be used to treat severe reactions.	It is essential to obtain a complete medical/drug/dental history from each patient and update at every encounter. The most common delayed reactions in a dental environment involve chemicals in latex gloves, topical anesthetics, other topical medications, disclosing solution.
Allergic Contact Dermatitis Associated with Latex Gloves	Type IV reaction; contact with residual chemicals used in the manufacturing of latex gloves	Langerhans cells ingest chemical molecules, present to the T lymphocytes, macrophages, and cytotoxic T cells, destruction of cells that contact chemical	Erythematic, pruritic, vesicular rash leading to dry cracked skin	Not applicable	Elimination of allergen, topical corticosteroids, anti-itch creams	It is essential to obtain a complete medical/drug/dental history from each patient and update at every encounter to discover this type of problem; avoid use of latex gloves.
Selective Immunoglobulin A Deficiency (SIgAD)	B lymphocytes are unable to produce IgA but levels of IgG and IgM are normal.	Often asymptomatic; may have respiratory or GI infections, a tendency for allergies, autoimmune diseases, and vascular disorders associated with the structure and function of collagen	Individuals may experience chronic sinus pain because of upper respiratory infections and deafness due to chronic ear infections.	Not applicable	Early diagnosis and aggressive treatment of the various infections	Clinicians should be aware of this disorder because IgA is found in saliva and other secretions and when there is a lack of IgA there is a higher risk of oral infections, possibly including caries. The patient should be informed of the risk and prevention strategies. Be aware that normal standard precautions for preventing the transmission of disease may not be effective and any contact with a pathogenic organism may cause a fatal infection.
DiGeorge Syndrome (Chromosome 22q11.2 Deletion Syndrome)	Genetic disorder caused by a deletion of DNA on chromosome 22	Disorder causes failure of the third and fourth pharyngeal pouches to develop, resulting in partial or total absence of the thymus, parathyroid glands, and the thyroid gland. T-cell level is low or absent, increasing susceptibility to infections; B-cell activity is diminished because T-cell activation is required.	Perioral effects include retro/micrognathia, facial malformation, cleft palate/lip, and microdontia. The patient may also have congenital heart defects, developmental delays, and/or learning disabilities. This individual is much more susceptible to viral and fungal infections.	Not applicable	Early diagnosis and aggressive treatment of the various infections and replacement of the missing hormones if necessary. Congenital heart defects and/or cleft lip/palate may require surgical intervention and dental treatment modifications.	Be aware that normal standard precautions for preventing the transmission of disease may not be effective and any contact with a pathogenic organism may cause a fatal infection.
Irritant Contact Dermatitis	Not a hypersensitivity reaction, caused by contact with irritating chemicals or mechanical irritation caused by friction	Typical inflammatory response to a local irritant	Erythematic, dry, itchy, rough skin; vesicle formation is unusual.	Not applicable	Eliminate the source of irritation, topical corticosteroids, anti-itch creams	Irritant and allergic dermatitis are very similar; medical evaluation may be needed to determine the correct diagnosis, and refer for definitive diagnosis if indicated.

CHAPTER 5

Neoplasia

KEY TERMS

Acromegaly	Immunotherapy
Alopecia	Incisional biopsy
Anaplasia	Ionizing radiation
Anemia	Keratinocytes
Anorexia	Labile cell
Apoptosis regulating gene	Leukopenia
Benign	Malignant
Benign nevus	Mammography
Biomarkers	Metastasis/metastatic/metastasize
Bone marrow suppression	Mitotic figures
Cancer grading	Mucositis
Carcinogenesis	Needle biopsy
Carcinogenic agent	Neoplastic growth/neoplasm/neoplasia
Carcinoma	Oncogene
Carcinoma in situ	Paraneoplastic syndromes
Chemocaries	Peritoneal cavity
Chemotherapy	Permanent cell
Chronic myelogenous leukemia	Peutz-Jeghers syndrome
Colonoscopy	Philadelphia chromosome
Colostomy	Pleomorphism
Deoxyribonucleic acid (DNA)	Pleural cavity
Differentiation	Polyps
DNA repair genes	Primary tumor
Dysphagia	Proto-oncogene
Embolus (emboli)	Radiation caries
Encapsulated	Radiosensitive
Epidermis	Sarcoma
Excisional biopsy	Seeding
Fine-needle aspiration	Stable (quiescent) cell
Gigantism	Thrombocytopenia
Hepatocellular carcinoma	Thrombocytosis
Hormone/antihormone therapy	Thrombus (thrombi)
Hyperadrenalism	Translocation
Hyperchromatic nuclei	Tumor staging
Hypercoagulation	Tumor-suppressor gene
Hyperthyroidism	

LEARNING OUTCOMES

1. Define and use the key terms discussed in this chapter.
2. Describe the difference between labile, stable, and permanent tissues.
3. Describe the basic principles of genetic control over cell growth.
4. Discuss how unregulated growth of cells resulting from genetic changes may occur.
5. Compare and contrast the characteristics of malignant and benign tumors.
6. Discuss genetic changes that have the potential to initiate neoplastic growth.
7. Discuss the five general etiologic factors involved in carcinogenesis.
8. Describe the local growth of malignant neoplasms.
9. Describe three mechanisms of metastasis.
10. List possible symptoms of neoplasia and the methods used to diagnose neoplastic growth.
11. Describe cancer grading and tumor staging, and state the importance of each in determining treatment and prognosis.
12. Describe the systemic effects of malignancy.
13. List the different types of cancer therapies available and describe how they work.
14. Describe the potential systemic and oral side effects of cancer therapy.
15. List measures an individual can take to lower the risk of developing cancer.
16. Describe the characteristics of the three most common skin cancers.
17. List screening methods for breast, prostate, and colorectal cancers.
18. Describe the symptoms of lung cancer.
19. Describe the typical appearance of metastatic cancer found in the oral cavity.
20. List the cancers most likely to metastasize to the oral cavity.

CHAPTER OUTLINE

Normal Cell Growth
Growth Categories
Growth Regulators
Neoplastic Growth
Benign Neoplasms
Malignant Neoplasms
Carcinogenesis
Local Growth and Distant Metastasis
Diagnosis
Tumor Grading and Staging
Systemic Effects of Malignancy
Cancer Therapies
Side Effects of Cancer Therapy
Prevention
Common Cancers
Basal cell carcinoma (BCC)
Squamous cell carcinoma (SCC)
Melanoma
Breast cancer
Prostate cancer
Lung cancer
Colorectal cancer
Oral metastatic cancer

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#10 Patient Education: UVA/UVB Skin Protection
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#19 Oral Health Care Management for the Patient with Cancer
#24 Tobacco Cessation
#27 Motivational Interviewing for Behavior Change

Normal Cell Growth

The cell is the basic unit of life. Cells make up tissues that form organs, which combine to form systems, and finally develop into a living organism. The growth of the organism is evidenced by the multiplication and growth of individual cells within the organism. While all cells within the body have the genetic ability to reproduce, they are not all allowed to do so. In fact, each type of cell within the body has a specific growth potential that is reached when the cell becomes mature. It will be helpful to review this information before discussing what happens when the mechanisms that regulate cellular growth go awry.

Growth Categories

Tissues of the body can be categorized into three major groups: labile, stable, and permanent, depending on the growth potential of their component cells. **Labile cells** are found in tissues that are constantly undergoing controlled, rapid reproduction to replace cells lost through normal wear and minor injury. The skin, mucous membranes, blood cell–forming tissues, and lymphoid tissues are examples of tissues composed of labile cells. In the skin and mucous membranes, epithelial cells rapidly reproduce to replace cells lost continuously throughout the day. The life expectancy of a normal red blood cell is approximately 120 days, after which it undergoes apoptosis, is removed from the body, and is replaced by another mature red blood cell formed in the bone marrow.

Stable or **quiescent** cells are found in tissues that do not usually undergo reproduction but can be triggered to do so under the right circumstances, such as after an injury. In this case, the cells are stimulated by growth factors manufactured by the injured cells and other cells surrounding the injured cells. The liver, kidneys, pancreas, smooth muscles, and vascular endothelium comprise stable cells. Liver cells do not usually replicate, but if traumatic damage does occur, the cells are triggered to start reproducing. For example, an individual receiving a liver transplant receives only a portion of the donor's liver. Not only does that portion grow to a normal size within the recipient, but the remainder of the donor's liver also regenerates to its normal size.

Permanent cells have reached their final differentiated form and are not capable of reproduction. These cells do not regenerate after injury. The tissues of the heart, skeletal muscle, and nervous system are examples of tissues made up of permanent cells. When the heart undergoes a traumatic event such as a heart attack or myocardial infarction (MI), the cells cannot reproduce to repair the injury. Scar tissue is formed, and the remaining heart muscle must take over the functioning of the damaged area, resulting in increased demand on the remaining tissue. In addition, depending on the extent of the injury, the individual would be at a higher risk for another MI or problems such as congestive heart failure. Currently, researchers are investigating the potential for using stem cells to repair some of these permanent tissues as well as for other purposes.

Growth Regulators

The growth potential of labile, stable, and permanent cells is genetically controlled. Genes, called **deoxyribonucleic acid (DNA)**, are the single units of inheritance that make up the chromosome. Specific genes called **proto-oncogenes** act to promote the growth of the cells in which they are contained. Each cell is also endowed with **tumor-suppressor genes** that produce substances to inhibit uncontrolled growth. Other genes regulate preprogrammed death of the cell or apoptosis. Additionally, **DNA repair genes** monitor the structural components of the DNA strand within each cell. If errors are found, these genes will attempt to repair them or mark the cell for destruction by apoptosis. If something interferes with any of these genetic controls, then neoplastic or new cellular growth may occur.

APPLICATION **5.1**

Stem Cells, Science Fiction or Reality?

There are two types of stem cells, embryonic stem cells that are obtained from the blastocyst (3- to 5-day-old embryo) and adult stem cells or somatic stem cells that are found in the bone marrow and possibly in muscle, brain, and other tissues. Embryonic stem cells can differentiate into any of the specialized cells in the body. These cells can be grown in the laboratory and remain undifferentiated for what is thought to be an indefinite amount of time. This enables the production of large amounts of stem cells that can be used for research purposes.

Adult stem cells are much harder to find within the tissues and do not reproduce as rapidly as the embryonic stem cells. Adult stem cells are much more directed in their development. In other words, there is a limit as to what type of cell the adult stem cell can differentiate into. For example, a stem cell found in the bone marrow may only be able to differentiate into a blood-forming cell and not a nerve cell. However, recent animal studies have suggested that some of these adult stem cells are more flexible than was once thought. Stem cells derived from umbilical cord blood are an example of adult stem cells captured at a "younger" stage than those harvested at any other time of life. Some believe these "younger" cells may have a higher potential for medical use than "older" cells. Recent research has focused on dental-derived stem cells due to their easy accessibility and high proliferative ability. Five different dental stem cells (periodontal ligament, dental follicle, cells from the apex of the root or apical papilla, and cells from the pulp tissues of both permanent adult teeth and primary exfoliating teeth) have been identified, and there is a possibility of discovering several more in the near future. All five of these stem cells have shown the potential to either produce or initiate the production of cells that create bone, muscle, cartilage, and adipose and nerve tissues in addition to regenerating all of the tissues of the periodontium. The potential for using stem cells that are easily harvested from the oral cavity for repairing, replacing, or regenerating the tissues of an individual without the need for a lifetime of immunosuppressive medications may become a milestone in medical research. To this end, much attention is being focused on providing appropriate storage for both cord blood and teeth.

Tooth banks and cord blood banks are readily available worldwide to store an individual's stem cells. The cord blood, teeth, or associated tissues are placed in cryogenic storage for 20 or more years or as long as the owner is willing to pay the storage fees. At this time, it is believed these tissues can be stored indefinitely as long as the proper conditions are maintained. The dental hygienist may be the person charged with explaining what dental stem cells are and why a parent or other individual might want to save and store them for future use.

Stem cells are being used to test the effectiveness of drugs or to determine whether drugs could harm specific types of cells. They are being used to develop drugs that target cells of a specific type. Stem cells have been used successfully to treat leukemia, lymphoma, and sickle cell disease (see Chapter 9, Blood Disorders) for many years. They have also been used to treat several types of immune disorders. Stem cells could be used to create tissues to replace or repair damaged or destroyed tissues, such as skin destroyed by burns or nerve tissues destroyed by a spinal cord injury. Dental stem cells have already been used to produce tooth-like structures in the laboratory, so it may not be too long before we have the ability to replace a missing tooth with a regenerated tooth derived from dental stem cells. Stem cells can be stimulated to differentiate into cells that secrete essential substances and could be the answer to finding cures for disorders such as Parkinson disease and diabetes. Research on stem cells could help determine what happens to make a normal cell become malignant or why some birth defects occur. One of the more important questions being looked at now relates to discovering what signals prompt the stem cells to reproduce and then to differentiate. In addition, researchers must discover what causes the stem cell to differentiate into a skin cell as opposed to a nerve cell or a liver cell (Stem Cell Information, 2011). As this edition is written, scientists have reported discovering how to turn a person's own cells into cells that act like embryonic stem cells. These so-called induced pluripotent stem (iPS) cells are reducing the need for human embryos in research and opening up exciting new possibilities for stem cell therapies (Genetic Science Learning Center, 2011). Stem cell research is not science fiction, it is reality and the dental profession will have a front row seat at the first show!

Neoplastic Growth

Neoplastic or unregulated growth occurs when a genetic change or mutation interferes with the regulation of normal cell growth. Neoplastic growth is not the same as hyperplasia because a permanent change in the regulation of cellular division, growth, or differentiation has occurred on the genetic level. Neoplasms express a wide range of characteristics that can be divided into two basic groups: benign and malignant. Table 5.1 provides a summary of the characteristics of benign and malignant neoplasms.

Benign Neoplasms

Benign neoplasms do not spread into adjacent tissues or metastasize to distant sites. These neoplasms normally, but not always, grow slowly by expansion and put pressure on surrounding structures and tissues. They are usually **encapsulated** (encased in a fibrous capsule) and move freely within the surrounding tissues. The surface of these lesions, if visible, may appear stretched, but it is usually normal in color. Benign neoplasms do not have an effect on the host unless they impinge on a nerve or vital organ or become very large, at which time pain, paralysis,

TABLE **5.1** **Comparison of the Characteristics of Benign and Malignant Neoplasms**

Characteristic	Benign	Malignant
Cell characteristics	Well-differentiated; resemble normal cells of the tissue of origin	Range of well to undifferentiated with little or no resemblance to the tissue of origin
Tumor growth	Localized expansion; usually encapsulated or otherwise separated	Infiltrates the surrounding tissues, becomes fixed to and not easily separated from them
Growth rate	Slow growth; mitotic figures are rare	Varies; the more undifferentiated the cells the faster the rate of growth; mitotic figures are common
Metastasis	None	Metastasizes through the blood and lymph to distant sites

APPLICATION **5.2**

Hyperplasia versus Neoplasia

Intraoral examples of the difference between hyperplasia and neoplasia can be seen in the following two cases. Case 1 involves leukoplakia associated with smokeless or spit tobacco and case 2 involves verrucous carcinoma, which is also associated with spit tobacco.

Both cases start as the individual begins to use the product. The mucosal site in which the tobacco is kept begins to undergo a change. The chemicals in the tobacco are toxic, and the body initiates a line of defense against them in the form of cellular adaptation. Eventually, after months or years, depending on the individual, the mucosal tissues in the area where the tobacco is kept start to show a clinical difference from the areas not in direct contact with the tobacco. The tissue becomes whiter (hence the name leukoplakia), more leathery, and eventually so thick the tissue starts to become fissured (Fig. 5.1). Leukoplakia is a clinical description for a white lesion not yet definitively diagnosed by biopsy. In this case, the leukoplakia is the clinical manifestation of mucosal hyperplasia. As the epithelial cell layer becomes thicker, the tissue becomes less transparent and more opaque or white. At this point, the two cases follow different paths.

In the first case, the hygienist discusses the area and the cause with the patient. The patient is shown the area and is asked if he wants to quit tobacco use. The patient decides tobacco cessation is the right thing to do at this time, and with the help of the dental team and support from family and friends, he is successful. The area of leukoplakia is kept under observation at each preventive maintenance appointment for the next 2 years. Slowly the hyperplastic area resolves, and after 2 years, the tissues are no different from the tissues that did not contact the tobacco. As in a true case of hyperplasia, once the stimulus was removed, the growth stopped and the lesion resolved over time.

In the second case, the hygienist follows the same protocol, but the patient does not want to stop using tobacco. The oral tissues where the tobacco is kept become more and more hyperplastic. Often, the hyperplastic change is accompanied by differing degrees of dysplasia. After years of constant tobacco use, the chemicals interfere with one or more genetic controls within the epithelial cells, and a neoplastic change occurs. After several more years, the hygienist notices a distinct change in the appearance of the lesion. It starts to become exophytic and verrucous or wart-like (Fig. 5.2). The patient is shown the area and asked again if he would like to quit tobacco. This time, he agrees and after months of hard work is successful in his attempt to quit. The dental team monitors the intraoral area during this time but does not notice any resolution; to the contrary, the lesion appears to be enlarging and becoming more exophytic. The patient is sent for a biopsy of the area, which returns with a definitive diagnosis of verrucous carcinoma. As expected, removal of the stimulus only stopped the hyperplastic lesion, not the neoplastic lesion. Verrucous carcinoma will be covered in detail in Chapter 16. See Clinical Protocols #24 and #27.

FIGURE 5.1. Leukoplakia associated with spit tobacco. This picture shows the characteristic white color and fissuring consistent with lesions of this type.

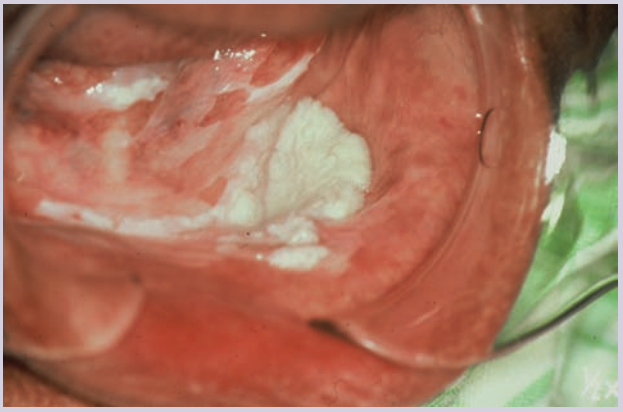

FIGURE 5.2. Verrucous carcinoma. Verrucous carcinoma associated with long-term spit tobacco use. Note the exophytic, thick, leathery growth and fissuring. (Courtesy of Dr. John Jacoway.)

loss of function, or even death may result. For example, a benign brain tumor can prove just as fatal as a malignant tumor, because it displaces and damages vital brain tissues. Often, benign endocrine gland tumors can cause the gland to hyperfunction and prove damaging to the host. Examples of this are **gigantism** and **acromegaly** caused by prepubertal and postpubertal hyperfunction of the pituitary gland, respectively (see Chapter 7). A histological study of a benign tumor will show well-**differentiated** cells that are the same as, or closely resemble, the cells of origin (Fig. 5.3A–C). Benign neoplastic cells maintain the genetic capability to remain differentiated but have somehow lost the genetic capability to stop unnecessary cellular replication. Terms that denote benign neoplasms usually contain the name of the tissue of origin and end in "-oma." Table 5.2 lists the nomenclature of benign and malignant tumors. Pictures of the following benign growths, granular cell tumor (Fig. 1.17), fibroma (Fig. 1.22), and papilloma (Fig. 1.35) can be seen in Chapter 1.

Malignant Neoplasms

Malignant neoplasms or cancers differ from benign neoplasms in many ways. However, the defining characteristics of malignant tumors are their ability to invade local tissues and to **metastasize** to distant sites. Malignant neoplasms usually grow more rapidly, and when they invade the surrounding tissue, it is difficult to determine where the tumor begins and the normal tissue ends. The tumor may appear fixed to underlying tissues when palpated, because the tumor has extended into the tissues and has not just pushed them aside. Histologically, cancer cells may be fairly well differentiated or mildly to severely undifferentiated and may bear little resemblance to the tissue of origin (Fig. 5.3C). Cancer is asymptomatic in its early stages. When symptoms do appear, they are varied and depend on the location and type of tumor involved. Many cancers can be successfully treated if detected in a timely manner. Malignant neoplasms are fatal if they remain undetected until they have metastasized throughout the body and cannot be treated or if they are allowed to progress with no treatment.

There are two general types of malignant neoplasm, **carcinoma** and **sarcoma**. In cancer nomenclature, carcinoma is applied to cancers arising from epithelial cells, for example, squamous cell carcinoma (SCC) and basal cell carcinoma (BCC). Likewise, sarcoma denotes a growth arising from connective tissues and sarcoma would be added to the name of the specific tissue of origin, for example, osteosarcoma or osteogenic sarcoma and fibrosarcoma. Cancer nomenclature is not consistent, and there are exceptions to the rules. For example, melanoma is a malignant growth of melanocytes, and a lymphoma is a malignant growth of

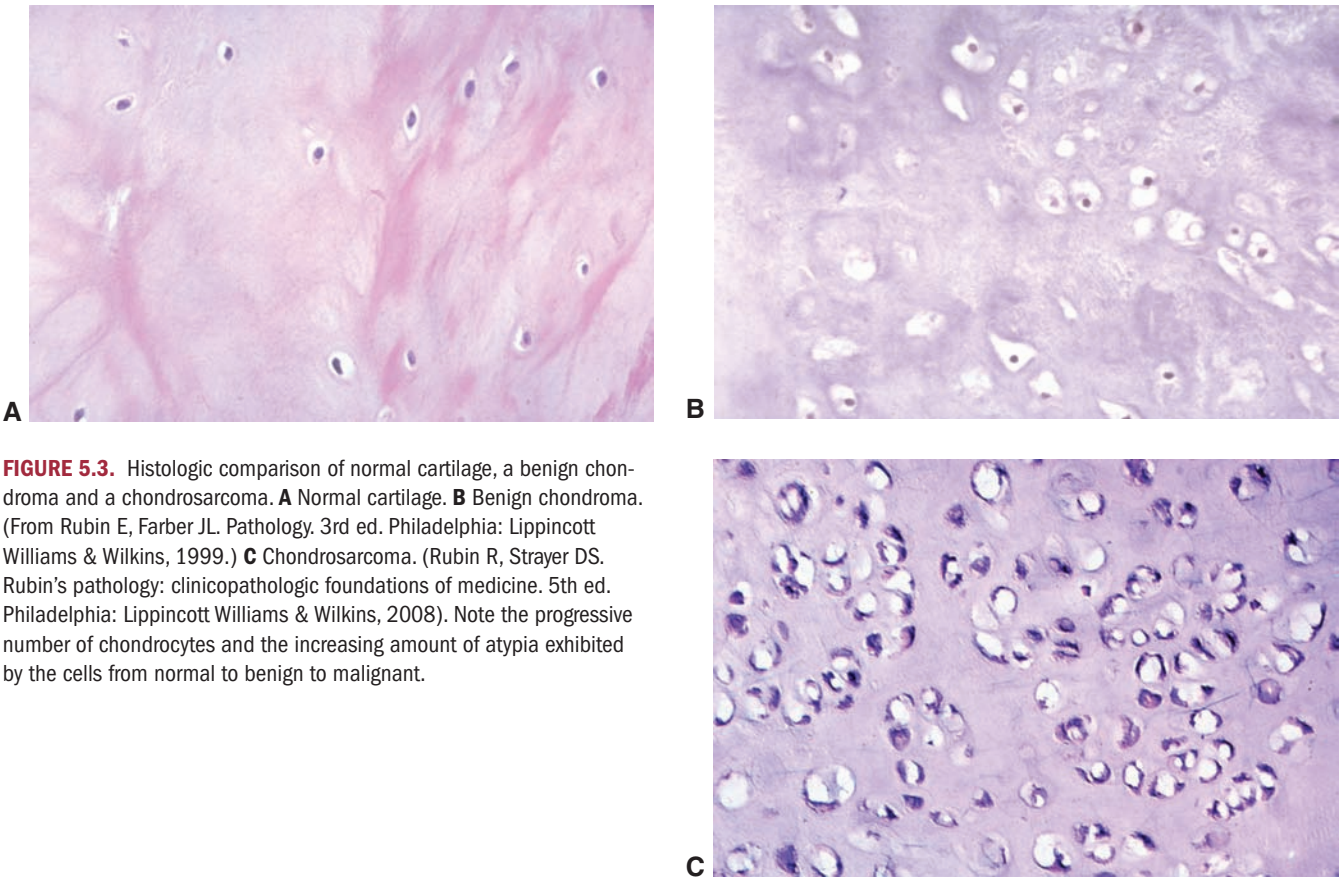

FIGURE 5.3. Histologic comparison of normal cartilage, a benign chondroma and a chondrosarcoma. **A** Normal cartilage. **B** Benign chondroma. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.) **C** Chondrosarcoma. (Rubin R, Strayer DS. Rubin's pathology: clinicopathologic foundations of medicine. 5th ed. Philadelphia: Lippincott Williams & Wilkins, 2008). Note the progressive number of chondrocytes and the increasing amount of atypia exhibited by the cells from normal to benign to malignant.

TABLE 5.2 Nomenclature for Benign and Malignant Neoplasms

Tissue of Origin	Benign Neoplasm	Malignant Neoplasm
Epithelial		
Epidermis	Squamous papilloma	Squamous cell carcinoma (SCC)
Glandular	Adenoma	Adenocarcinoma
Melanocytes	Nevus	Melanoma
Nervous		
Nerve sheath	Neurilemmoma	Neurilemmal sarcoma
Nerve cell	Neuroma	Neuroblastoma
Glial cells	Glioma	Glioblastoma
Blood		
Red blood cells		Erythrocytic leukemia
Plasma cells		Multiple myeloma
Lymphocytes		Lymphocytic leukemia or lymphoma
Connective		
Bone	Osteoma	Osteosarcoma
Cartilage	Chondroma	Chondrosarcoma
Adipose	Lipoma	Liposarcoma
Fibrous	Fibroma	Fibrosarcoma
Blood vessels	Hemangioma	Hemangiosarcoma
Lymph vessels	Lymphangioma	Lymphangiosarcoma
Muscle		
Smooth	Leiomyoma	Leiomyosarcoma
Striated	Rhabdomyoma	Rhabdomyosarcoma

lymph cells, and neither is benign as their names would appear to signify. The name "leukemia" would imply a white blood cell deficiency, while in fact leukemia is a malignant growth of white blood cells; there is no benign growth of white blood cells. Other cancers are named for the person who first diagnosed them; for example, Thomas Hodgkin (1798–1866), an English physician, first diagnosed Hodgkin disease.

Carcinogenesis

Carcinogenesis is the development or process of cancer growth. Genetic damage or mutation is the foundation of carcinogenesis. Proto-oncogenes, tumor-suppressor genes, DNA repair genes, and genes that regulate apoptosis are needed to control the cellular growth cycle. Any damage to these genes will upset the delicate balance between cell growth and death.

- **Proto-oncogene**—Mutated proto-oncogenes become **oncogenes**. The oncogene encourages or accelerates the growth of a particular cell. The most common proto-oncogene mutations involve the alteration of just one or two base pairs in the DNA strand. Another type of mutation involves the **translocation** of genetic material from one chromosome to a different chromosome. Ninety five percent of individuals with **chronic myelogenous leukemia** (see Chapter 9) carry the **Philadelphia chromosome**, which results from the incorrect fusion of parts of two different chromosomes causing the production of an abnormal protein promoting overproduction of the white blood cell precursors or myeloid cells seen in this disease. A mutation may involve the creation of multiple copies of a particular gene. For example, approximately 30% of breast cancers involve cells containing multiple copies of the human epidermal growth factor receptor-2 (HER-2/neu) gene. The overexpression of the gene causes the production of excessive amounts of growth factor, resulting in aggressive tumors with poor outcomes.
- **Tumor-suppressor genes**—These genes inhibit the growth of cells with DNA damage and initiate repair by DNA repair genes or identify cells for apoptosis if they cannot be repaired. There are a number of different genes considered to be tumor suppressors. The *p*53 gene is one of the most important; often called the "guardian of the genome," it is the most common target for genetic mutation in human cancers (Porth, 2011). Other examples of tumor-suppressor genes are the BRCA1 and BRCA2 (breast cancer 1, 2) genes. Women who have mutated BRCA1 or 2 genes have a significantly increased risk of both breast and ovarian cancers. When tumor-suppressor genes are inactivated by genetic mutation, cell division and growth can proceed unregulated.

- **DNA repair genes**—These genes form a line of defense against genetic mutations. They are contained in the genetic material of every cell, where they watch over the integrity of the DNA and regulate the repair or destruction of the involved cells. If these genetic functions are lost, the cells with errors in their DNA will be allowed to replicate. If the errors involve a neoplastic change, neoplastic growth (whether benign or malignant) will be allowed to occur.
- **Apoptosis regulating genes**—Tumors occur not only from unregulated growth of cells but also from cells that are able to evade apoptosis or death. Mutations in genes that regulate apoptosis could result in the formation of "immortal" cells. Reduced cell death also results in the formation of a tumor.

Cells may acquire genetic damage in a number of ways including inherited traits or influences, chemical exposures, environmental insults, viral infections, and immune system defects, among others. In most cases, there is not one cause but many different events or insults that have occurred and accumulated over the life of the individual. Some of these are listed below:

- Inherited traits or influences—Mutations in tumor-suppressor genes are most often related to inherited forms of cancer. About 50 types of cancer have a genetic predisposition. Breast cancer, for example, is more likely to occur in women who have a history of breast cancer in their families. Individuals who have inherited Gardner syndrome (see Chapter 19) have a higher than normal risk of developing colorectal cancers.
- Chemical exposures—In many cases, exposure to the chemical agent is consistent over a long period of time. For example, smoking exposes the individual to many chemicals known to cause cancers of the lung and larynx. Esophageal, pancreatic, and bladder cancers have also been associated with tobacco use. Many of our food products contain added nitrates as a preservative. Nitrates may be converted into nitrosamines in our digestive tracts. Nitrosamines have been implicated in cancer development because they are known to produce cancer in rodents. Many other chemicals have been shown to cause cancers in humans and animals. Box 5.1 provides a list of some of the more common chemical **carcinogenic** (cancer causing) **agents**.
- Environmental insults—Environmental agents have also been linked to cancer in humans. Many skin cancers are caused by exposure to ultraviolet light from the sun. Ultraviolet radiation causes a specific type of DNA damage no other carcinogenic agent has been shown to cause. This damage is cumulative, and damage during early years of life may result in cancer later in life. Asbestos, used for many construction needs, is associated with mesothelioma, or cancer of the **pleural** (lung) and **peritoneal** (abdominal) **cavities**. While mesothelioma is rare in the general population, workers who were exposed to asbestos over many years have a 3% or more chance of developing this cancer (Rubin & Strayer, 2012).
- Viral infection—Viruses that have the ability to cause cancer are called "oncogenic viruses." Viruses enter the host cells and use the cell's replication mechanisms to reproduce viral particles. To accomplish this, the virus integrates some of its DNA into the host cell's DNA. This altered DNA becomes oncogenic, or cancer causing. Certain strains of human papilloma virus (HPV) have been shown to cause cervical and anogenital SCC and have been increasingly associated with oropharyngeal cancers. Epstein-Barr virus (EBV) has been associated with several types of cancer including Burkitt lymphoma, nasopharyngeal cancer, and Hodgkin disease. Human herpes virus (HHV 8) is associated with Kaposi sarcoma seen in AIDS. Hepatitis B (HBV) and C (HCV) viruses have both been implicated in **hepatocellular carcinoma** (liver cancer) when the individual is a chronic carrier of either disease.
- Immune system defects—Immune system defects may also be associated with a higher risk of cancer. Studies are under way to determine if parts of our immune system can protect us from malignant neoplastic growths. Many of the studies are focusing on the ability of T cells, natural killer cells, and macrophages to destroy tumor cells. An immune defect affecting any of these cells may increase the individual's risk for cancer. Most of the evidence pointing toward a possible immune system role in cancer prevention has been associated with the fact that immunocompromised individuals are more likely to develop malignancies than their healthy counterparts. For example, Kaposi sarcoma and lymphoma are commonly seen in patients with AIDS.

BOX 5.1 Chemicals Associated with a High Risk of Cancer

- Alcohol
- Vinyl chloride
- Diethylstilbestrol
- Benzene
- Arsenic
- Formaldehyde
- Nickel compounds

Local Growth and Distant Metastasis

Malignant tumors do not magically appear. They start out with a single mutated cell that has evaded all of the body's defense mechanisms. This starts a sequence of changes that may begin with dysplasia and end with an invasive neoplasm that eventually metastasizes to distant sites (Fig. 5.4). In the case of epithelial cancer or carcinoma, the dysplastic cells are separated from the surrounding tissues by the basement membrane (Fig. 5.5). Carcinoma in this early stage is called **carcinoma in situ** and can be readily treated and cured. If left untreated, the tumor cells will penetrate the basement membrane using one or more of the mechanisms discussed

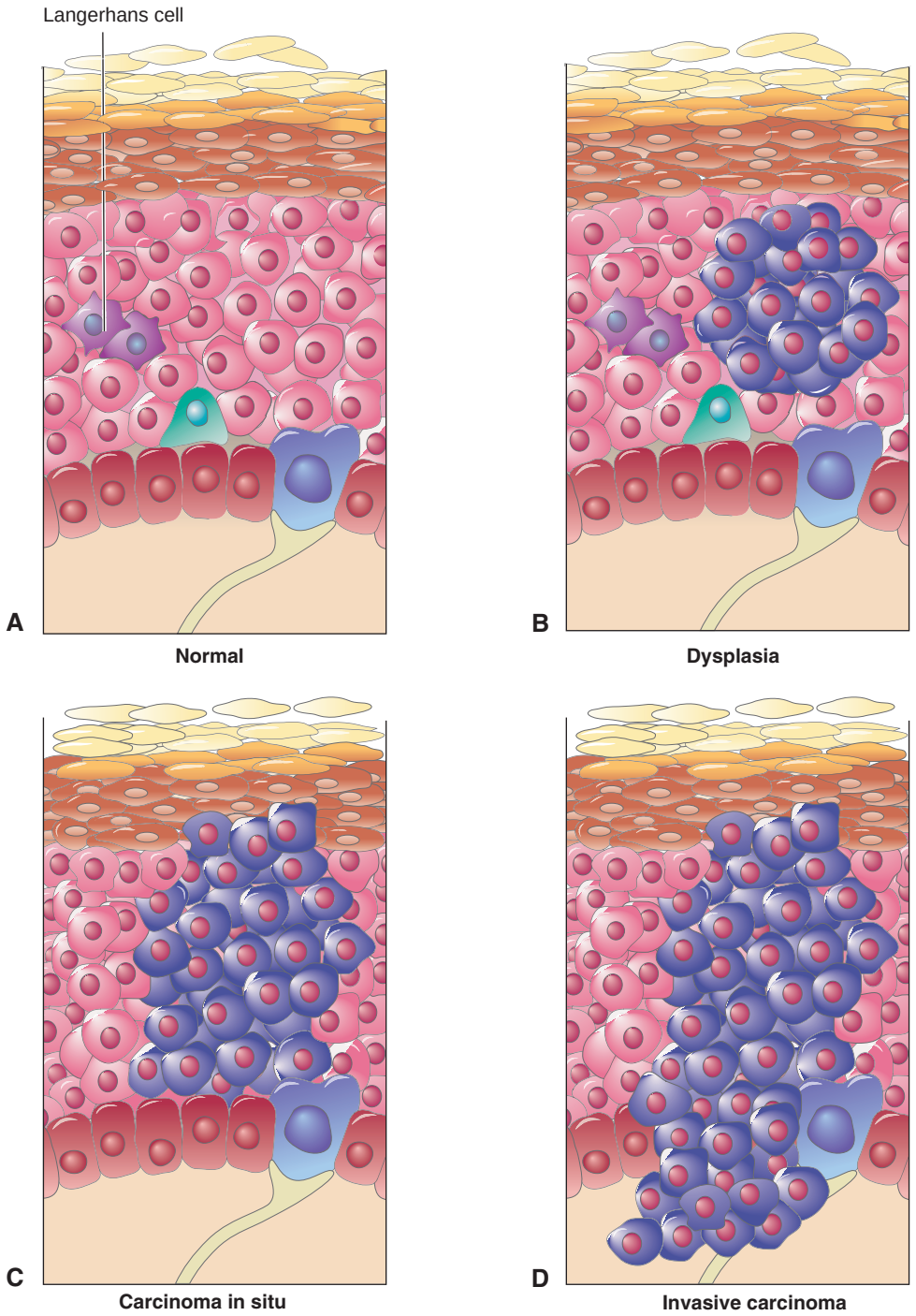

FIGURE 5.4. Progressive changes from adaptive dysplasia to neoplasia. **A.** Normal epidermis with intact basement membrane. **B.** Epidermis showing dysplastic changes. **C.** Severe dysplasia or carcinoma in situ. Note the basement membrane is still intact. **D.** Invasive neoplasia. The basement membrane has been breached.

below and extend into the surrounding tissues (Fig. 5.6). Other types of cells, such as connective tissue or nervous tissue cells, do not have a defined in situ stage because they do not have a basement membrane. Once tumor cells have extended into the local tissues, there is an increased risk of lymph node involvement and metastasis to distant sites. Malignant tumors are able to spread into the surrounding tissues by use of several mechanisms.

- Mechanical pressure—As tumors grow, they can exert mechanical pressure on normal cells in the area disrupting their nutrient supply, which weakens or destroys them enabling the cancer cells access to the surrounding tissues.
- Enzymes—Cancer cells are able to produce enzymes allowing them to destroy collagen and in turn weaken the extracellular substances holding normal tissue cells together, thereby allowing the spread of the cancer cells.

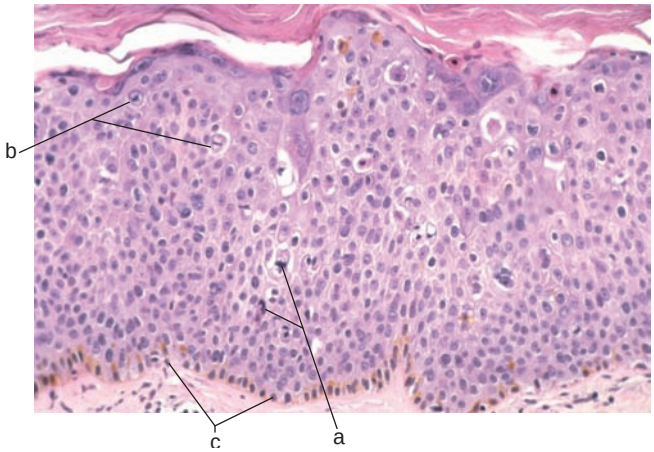

FIGURE 5.5. Squamous cell carcinoma (SCC) in situ. The entire epidermis is replaced by atypical keratinocytes. Multinucleation of the keratinocytes (*a*) and numerous mitotic figures (*b*) are apparent, but the basement membrane (*c*) is intact. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

FIGURE 5.7. Metastatic breast cancer. Breast cancer has metastasized to the area superior to the left orbit, causing ptosis or sinking of the eye. (From Tasman W, Jaeger E. The Wills Eye Hospital atlas of clinical ophthalmology. 2nd ed. Baltimore: Lippincott Williams & Wilkins, 2001.)

- Lack of adhesion—Cancer cells, especially of epithelial origin, do not adhere to each other as tightly as normal cells; therefore, they break off from the primary tumor and actually move into the surrounding tissues.

Other events must occur before tumor cells can establish a secondary tumor or metastatic site (Fig. 5.7). The tumor cells must penetrate the basement membrane, if there is one, and move through the cells of the surrounding tissues until entering either a lymph or blood vessel. The most common method of tumor spread is through the lymphatic system. Tumor cells entering a lymph vessel will travel to the regional lymph nodes and may establish a secondary tumor within one or more nodes. Eventually, these cancer cells will enter the circulating blood by way of the venous drainage of the lymphatics. Metastasis through blood vessels is more complicated because the tumor cells must first invade the vessel, usually a capillary or venule, and circulate through the vessels until finding a place to attach to the vascular endothelium. Then, the tumor cells must move through or breach the endothelium again before beginning to multiply in the new site. Body cavities may also provide an avenue for tumor metastasis. When tumors arise in the abdominal organs or the lungs, cancer cells may break off from the **primary tumor** (the initial or original site of neoplastic growth) and travel through the spaces to grow in adjacent organs. The process of tumor spread through the body's cavities is called **seeding** (Fig. 5.8).

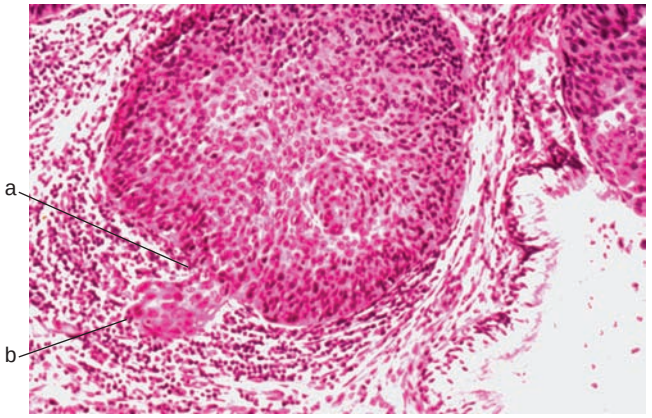

FIGURE 5.6. Microinvasive squamous cell carcinoma (SCC). Cancer cells have used mechanisms to destroy normal cells to breach the basement membrane of this gland (*a*) and spread into the adjacent tissues (*b*). (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

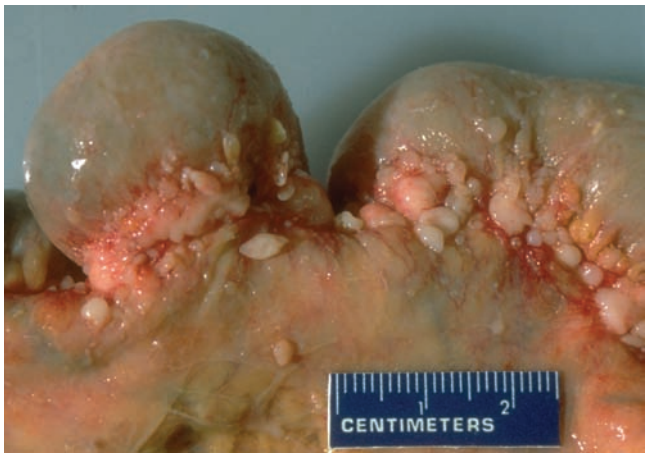

FIGURE 5.8. Seeding. Metastatic spread of ovarian cancer throughout the peritoneal cavity by means of seeding. Note the multiple small nodules of cancer studding this section of mesentery and small bowel. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

Diagnosis

The presence of a neoplasm may be suspected for many reasons. The individual may have symptoms related to the anatomic area in which a tumor is growing. **Dysphagia**, or difficulty swallowing, would occur with an esophageal tumor. Loss of memory might occur with a brain tumor. Other symptoms may relate to the tissue that is affected. A thyroid tumor might cause symptoms of **hyperthyroidism**, excessive production of thyroid hormone, while an adrenal tumor causes symptoms associated with **hyperadrenalism**, excessive production of cortisol (both are discussed in Chapter 7). Small tumors may remain undetected until they metastasize and the secondary tumors produce symptoms. Many cancers metastasize to bone tissue; therefore, bone pain may be the initial symptom of a primary tumor unrelated to bone.

Tumors may be discovered through a screening process. Common cancer screening methods include **colonoscopy,** skin examination, mammography, prostate examination, blood tests, and oral cancer screening examination. Blood tests are done to detect the presence of **biomarkers**. Biomarkers are chemicals produced by specific types of cancer cells or substances released by normal cells in response to cancer. For example, prostate cancer cells produce prostate-specific antigen (PSA). If an elevated level of this marker is found in the blood, additional testing should be done to determine if a prostate tumor exists. Lung and breast cancers may produce carcinoembryonic antigen (CEA); an elevated level of this substance would require further testing to rule out the presence of cancer in these areas. Promising new methods of screening are being developed; one such method uses saliva to detect several cancers including breast, head and neck, and oral cancer.

The most common sites for oral cancer to develop are listed in Box 5.2. All of these sites are visible to the dental hygienist, and unidentified lesions should be evaluated in office or referred for evaluation by another medical or dental professional. Some suspicious areas in the oral cavity may be screened using a technique called "brush biopsy," which uses a stiff circular brush to scrape cells from small oral lesions of unknown etiology (Fig. 5.9). Clinical Protocol #12 describes this and other adjunctive screening devices available to the dental community. In addition, all patients (especially those patients at high risk for developing oral cancer) should be shown how to examine their own mouths for signs of abnormal soft tissues. Clinical Protocol #11 suggests guidelines for training the patient to do this examination. In all cases, regardless of the symptoms or level of tumor markers, the final determination of a benign or malignant tumor must be made at the microscopic level.

BOX 5.2

Most Common Sites for Oropharyngeal Cancer Development

- Tongue (posterior lateral border and base)
- Tonsil
- Oropharynx
- Lip
- Minor Salivary glands
- Other sites: gingiva, buccal mucosa, floor of the mouth, soft palate

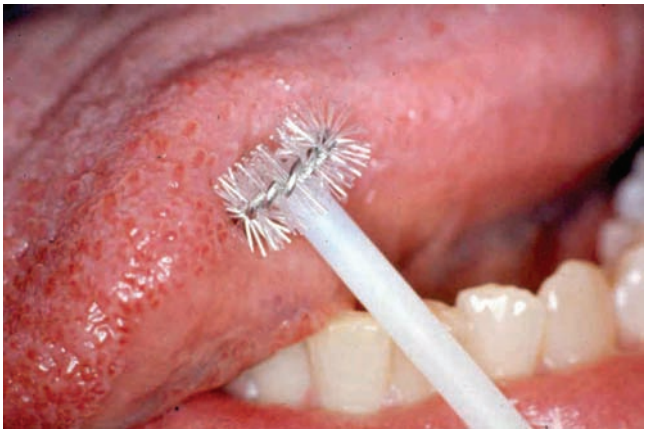

FIGURE 5.9. Brush biopsy. This is an example of using the brush biopsy technique to obtain cells from a lesion on the lateral border of the tongue. (Photo provided by CDx Laboratories, Inc., Suffern, NY.)

There are several methods of obtaining tissue cells for microscopic examination.

- **Excisional biopsy** removes the entire neoplasm and a wide margin of normal-appearing tissue surrounding it.
- **Incisional biopsy** involves the removal of a small piece of a large or inaccessible tumor including some normal-appearing cells from the edge of the tumor.
- **Needle biopsy** uses a large-bore needle to remove a core of tissue from a tumor; use is limited because of small sample size.
- **Fine-needle aspiration** involves removal of tumor fluid through a small-diameter needle; use is limited to tumors having a fluid component.

All biopsy specimens require an adequate and representative sample of the suspect cells in order to be useful. The margins of the specimens submitted with incisional and excisional biopsies are carefully examined for the presence of cancer cells. If the margins are not clear, cancer cells may remain. This finding will alter the course of treatment and the prognosis of the disease. Positive results indicating cancer are usually reliable; however, negative results may have to be followed up with a more invasive procedure to definitively rule out a malignancy.

Benign and malignant neoplasms are definitively diagnosed by microscopic evaluation of their cellular makeup. The cells of benign neoplasms are usually well differentiated and closely resemble the cells of origin. Benign tumors will not exhibit extension into, or fixation to, the surrounding tissues and, by definition, none will have metastasized to distant sites.

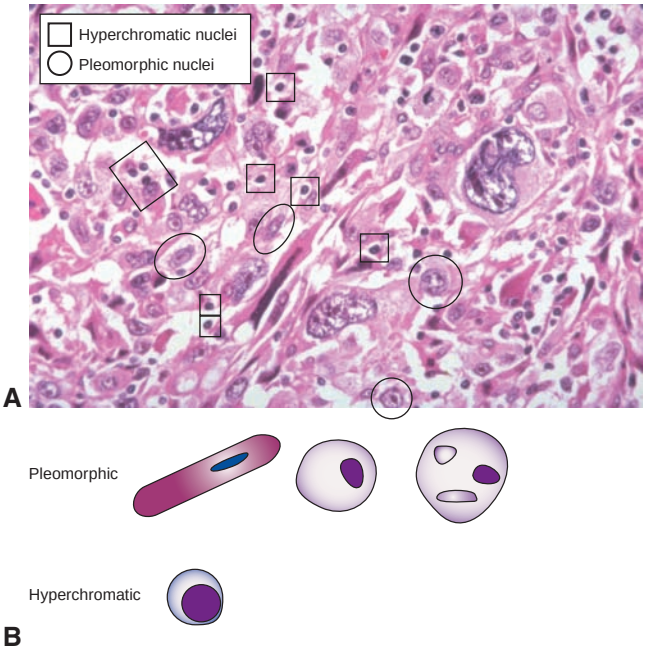

FIGURE 5.10. Anaplastic changes. **A.** Actual histology slide showing pleomorphic cells (*circled*) and cells with large, hyperchromatic nuclei (*boxed*). (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.) **B.** Illustration depicting pleomorphism and large hyperchromatic nuclei.

The cells of malignant neoplasms manifest a wide range of levels of differentiation, from relatively well differentiated to severely undifferentiated, or **anaplastic**. The more anaplastic the cells, the more aggressive the tumor is likely to be. **Pleomorphism** (a change in the size and shape of the cells and their nuclei) and **hyperchromatic nuclei** (darkly stained nuclei) are examples of the types of anaplastic changes seen in malignant cells (Fig. 5.10). In addition, malignant neoplasms will exhibit numerous **mitotic figures**, signifying high rates of cellular division and rapid growth (Fig. 5.11). Malignant tumors will extend into the surrounding tissues, making it difficult to find a boundary between tumor and normal cells. Finally, evidence of tumor cells in the regional lymph nodes or of distant metastasis clearly indicates the tumor is malignant.

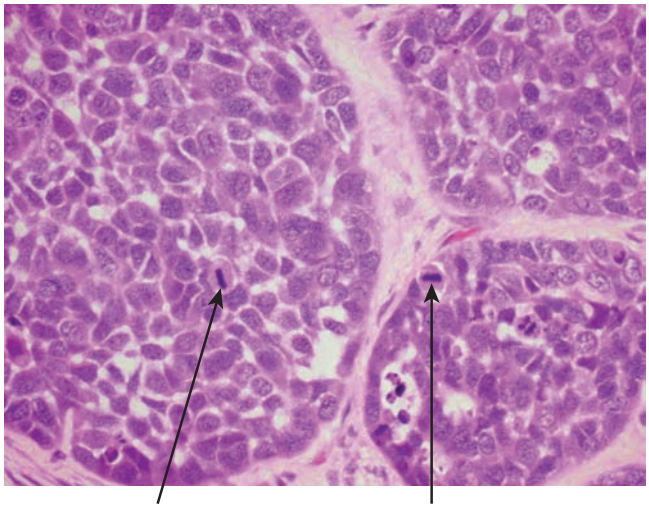

FIGURE 5.11. Mitotic figures. Numerous mitotic figures (*arrows*) signify rapid growth in this squamous cell carcinoma. (Courtesy of Yi-Shing Lisa Cheng.)

Tumor Grading and Staging

To determine the probable clinical course or outcome of a malignancy and help choose appropriate therapy, physicians use a **cancer grading** and staging system. Cancer cells are graded according to their level of differentiation and the number of mitotic figures in a given tissue sample. The cells are ranked from grades I to IV, with each level representing a greater lack of differentiation, or anaplasia, and increasing numbers of mitotic figures. It is presumed higher cancer grades are associated with more aggressive tumors, but this is not always the case.

Tumor staging is used to determine the extent of the disease. Several cancer staging systems are in use at this time, including the TNM system (T, size of the primary tumor; N, lymph node involvement; M, metastasis), developed by the International Union Against Cancer, and the AJC system, developed by the American Joint Committee on Cancer. The TNM system has a specific set of criteria for each organ or cancer site in the body. Refer to Box 5.3 for the coding information necessary to determine the TNM for epithelial cancers of the lip and oral cavity. The AJC system groups the information from the TNM together to determine an anatomic stage/prognostic group. Table 5.3 provides an example of how TNM information is grouped into these stages. Stage 0 includes all findings of carcinoma in situ. Treatment for this stage of cancer is rather conservative, depending on the grade of the cancer, and may involve surgical removal of the tumor and a wide margin of the surrounding normal tissue. As the stage increases numerically, the prognosis becomes worse, treatment becomes more difficult, and treatment options become less numerous (Edge et al., 2010). Surgery may no longer be an option if cancer has invaded vital structures of the head and neck area, and if metastasis has occurred, chemotherapy may be the only option to prolong survival and maintain an adequate quality of life for as long as possible.

Very promising techniques including molecular diagnosis and molecular profiling of tumors are beginning to be used to diagnose and predict the behavior of tumors. These techniques are leading to more individualized treatments and more predictable outcomes for many patients with cancer. It is hoped they will eventually lead to the development of new drugs targeting genetic and other molecular abnormalities specific not only for the type of cancer involved but also for each individual with cancer.

Systemic Effects of Malignancy

Systemic effects of malignancy not directly related to tumor invasion or metastasis are collectively called **paraneoplastic syndromes.** It is important to be familiar with these

BOX **5.3** **Definitions of TNM**

Lip and oral cavity (nonepithelial tumors such as those of lymphoid tissue, soft tissue, bone, and cartilage are not included)

Primary tumor (T)

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor 2 cm or less in greatest dimension
T2	Tumor more than 2 cm but not more than 4 cm in greatest dimension
T3	Tumor more than 4 cm in greatest dimension
T4a	Moderately advanced local disease[a] (lip) Tumor invades through cortical bone, inferior alveolar nerve, floor of mouth, or skin of face, that is, chin or nose (oral cavity) Tumor invades adjacent structures only (e.g., through cortical bone [mandible or maxilla] into deep [extrinsic] muscle of the tongue [genioglossus, hypoglossus, palatoglossus, and styloglossus], maxillary sinus, skin of face)
T4b	Very advanced local disease Tumor invades masticator space, pterygoid plates, or skull base and/or encases internal carotid artery

Regional lymph nodes

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in single ipsilateral lymph node, 3 cm or less in greatest dimension
N2	Metastasis in single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension; or in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension; or in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
N2a	Metastasis in single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension
N2b	Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension
N2c	Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
N3	Metastasis in a lymph node more than 6 cm in greatest dimension

Distant metastasis

M0	No distant metastasis
M1	Distant metastasis

[a]Note: Superficial erosion alone of bone/tooth socket by gingival primary is not sufficient to classify a tumor as T4.

Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the AJCC Cancer Staging Manual, Seventh Edition (2010) published by Springer Science and Business Media LLC, www.springer.com.

syndromes because they may be the first sign something is wrong. One or more of the following elements can occur by itself or in conjunction with any of the other elements.

- Fever of unknown origin, caused by the release of pyrogens by the tumor cells and interleukins by inflammatory cells in the area, often occurs, especially with osteogenic sarcoma and Hodgkin disease.
- Extreme weight loss and **anorexia** are very common to all cancer patients. The reason for this weight loss is not clearly understood but may be associated with an increased metabolic rate that occurs with malignancies.

TABLE **5.3** **AJCC Cancer Staging Manual Anatomic Stage/Prognostic Groups (Lip and Oral Cavity)**

Stage Grouping	Primary Tumor	Regional Lymph Nodes	Distant Metastasis
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1–3	N1	M0
Stage IVA	T4a	N0	M0
	T4a	N1	M0
	T1–3	N2	M0
	T4a	N2	M0
Stage IVB	Any T	N3	M0
	T4b	Any N	M0
Stage IVC	Any T	Any N	M1

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APPLICATION **5.3**

Molecular or Genetic Profiling

Since cancer is a genetic disease caused by defective deoxyribonucleic acid (DNA), researchers are developing ways to look at the genetic personality of the tumor through molecular profiling. Molecules that predict the behavior of cancer are called biomarkers. The presence or absence of biomarkers affects the way cancer is treated. Molecular profiling helps to identify biomarkers that can be helpful in determining a patient's prognosis and predicting the results of treatment. For example, molecular profiling shows about 50% of breast cancers are determined to be estrogen receptor positive and node negative (not found in the lymph nodes). The typical treatment is surgery with or without radiation therapy and then hormone therapy with drugs that reduce the level of estrogen. Most of these patients are offered chemotherapy to further reduce the chance of recurrence. Many of these patients may go through the devastating side effects of chemotherapy without knowing if, in fact, they were actually at risk for a recurrence. Researchers are developing new gene and molecular profiling tests that have the potential to answer this and other questions. In addition, as more of these biomarkers are identified and their functions uncovered, there is the potential for developing drugs that target the biomarker effectively, turning the function off or on and thus increasing the effectiveness of cancer therapies.

- Endocrine imbalances are common and can be caused by hypersecretion of tumors of the endocrine glands or overstimulation of the endocrine glands by tumor byproducts. Hypocalcemia (low calcium levels) and Cushing syndrome (hyperadrenalism, Chapter 7) are the most common paraneoplastic syndromes (Kumar et al., 2007).
- **Anemia** is another common problem associated with malignancies. Anemia can be caused by chronic bleeding, malnutrition, and malignancies of the blood-forming tissues.
- **Thrombocytosis** (platelet count over 400,000) and **hypercoagulation** problems may cause blood clots or **thrombi** to form that can obstruct vital vessels or produce **emboli** that may obstruct vessels in distant areas.
- Neurologic problems can result in varying degrees of motor and sensory dysfunction and may cause peripheral neuropathy, weakness, vision loss, seizures, and balance disorders.

These syndromes are not common; however, when they are present they can complicate care for the patient and have an overwhelming effect on the patient's psychologic outlook and quality of life.

Cancer Therapies

The major cancer therapies are surgery, radiation, and chemotherapy. The choice of an appropriate therapy or combination of therapies is based on the characteristics of the neoplasm, such as the type (carcinoma or sarcoma), stage, and location; the characteristics of the patient, such as age, sex, health status; and the patient's preferences. Determining treatment options for neoplasms in the head and neck area can prove very challenging because of the number of vital structures involved, the importance of maintaining adequate function, and sparing tissues to provide adequate opportunities for some degree of aesthetic reconstruction if necessary and possible. Surgery is the initial therapy for many cancers.

If the neoplasm is discovered in an early stage and is small enough, an excisional biopsy might be performed. If it is determined to be malignant, the margins of normal-appearing tissues will be thoroughly examined for any evidence of malignant cells. If none are found, there may not be any further therapy indicated, or radiation or chemotherapy might be used to try to ensure complete elimination of any remaining malignant cells. Surgical procedures for larger neoplasms, especially in the head and neck area,

APPLICATION **5.4**

Oral Health and Cancer Therapy

Aside from providing each patient with a thorough examination to detect possible oral cancers, the dental professional plays an important role in caring for patients who are facing cancer treatment or are undergoing cancer therapy. The extent of this role will be determined in part on the location of the cancer and the type of therapy involved. All cancer patients should have a dental evaluation prior to radiation to the head and neck area and prior to any type of chemotherapy. It is extremely important with any cancer therapy to maintain a healthy oral environment. Healthy oral tissues will decrease the potential for extreme oral side effects and infections resulting from normal oral bacteria. The dental hygienist's main role will be in educating the patient about what to expect and how to deal with some of the oral side effects. In addition, the hygienist may be called upon to help construct custom fluoride trays for the patient. These fluoride trays should be used during chemotherapy and during and after radiation therapy that places the salivary glands in the target area. (See Clinical Protocols #13 and #19.)

can be very complicated and are often combined with other therapies to help ensure the malignant cells are eliminated if possible.

Radiation therapy, often combined with surgical procedures, is used to destroy cancer cells and to attempt to avoid damage to surrounding normal structures. **Ionizing radiation** damages the DNA in malignant and normal cells. Rapidly dividing cells, such as cancer cells, are especially **radiosensitive**, or able to be injured or destroyed by radiation. A problem occurs with radiation because other types of rapidly dividing normal cells exist in the body, and radiation will affect these cells also if they are in the field of radiation. Epithelial and mucosal cells are the most likely type of cells to be harmed by ionizing radiation, resulting in many side effects, some irreversible.

Chemotherapy is used to destroy cancer cells in several ways. Some treatments interfere with the production of essential cellular components, and others disrupt DNA in both resting and dividing cells. Most often, a combination of chemotherapeutic drugs is used to increase the potential for destroying all of the cancer cells. Like radiation therapy, most chemotherapy drugs target rapidly dividing cells. Chemotherapy drugs are very toxic and will affect both normal and malignant cells. The associated side effects of chemotherapy are often unpredictable and can be very intense. While most of the side effects of chemotherapy are reversible, irreversible damage is possible.

Other forms of therapy such as hormone therapy, immunotherapy, antiangiogenesis therapy, photodynamic therapy (PDT), and hyperthermia are also being used. **Hormone or antihormone therapy** is being used for tumors that require hormones for growth or for those that will not grow in the presence of specific hormones. For example, some breast cancers depend on estrogen for growth; thus, giving an estrogen-blocking drug can impair growth of the tumor. To the contrary, prostate cancer cells will not grow well in the presence of estrogen, and estrogen therapy is often used to stop the growth of these tumors. Much research is being done in a new area of treatment called **immunotherapy**, which takes advantage of the body's own immune system to destroy cancer cells. Tumor-specific vaccines that will initiate a T-cell immune response against a tumor are being developed. Researchers are also using antibodies to target certain proteins found on specific cancer cells. Once the antibodies attach to these proteins, the cell is marked for destruction by the immune system. Targeting only the cancer cells with the specific protein spares normal cells that do not exhibit this protein. Most of the substances being developed for this type of treatment are being tested in combination with standard chemotherapeutic agents to maximize their effects. Antiangiogenesis therapy prevents or inhibits the growth of blood vessels that supply a tumor with nutrients. PDT uses a light source to activate a chemical substance that was delivered to the cancer cells either through the blood stream or by topical application to the surface of the skin. The light causes the chemical to react with oxygen within the cancer cell to create a substance that destroys the cell. Hyperthermia uses directed heat to destroy cancer cells or to make them more vulnerable to chemotherapy or radiation therapy.

BOX 5.4 Complementary Therapy or Medications

Complementary Therapies

- Acupuncture
- Meditation
- Art therapy
- Massage therapy
- Prayer/spirituality
- Yoga
- Tai chi
- Biofeedback
- Aromatherapy
- Music therapy
- Herbal or botanical medicines
- Diet and nutritional changes
- Hypnosis
- Tobacco use cessation

Complementary and alternative therapies help many patients manage their disease on a physical as well as psychologic and spiritual level. Complementary therapies focus on pain relief and managing the side effects of therapy, including the psychologic aspects. Alternative therapies are unproved treatments sometimes offered as cures. Some alternative therapies may help patients deal with their disease, but only in combination with accepted treatment methods. Box 5.4 provides examples of some of the more common complementary therapies available.

Side Effects of Cancer Therapy

Each cancer therapy has many potential side effects. Whether or not an individual experiences specific side effects depends on the extent of the therapy and the individual's response to the therapy. Surgical side effects include complete or partial loss of function, form, or aesthetics, depending on the extent and area of surgical intervention.

Radiation side effects are related to the area irradiated and the amount of radiation received. Because radiation affects rapidly dividing cells, the mucosal cells of the gastrointestinal tract are at high risk. One of the most common mucosal side effects is **mucositis**, which manifests as painful ulcerations. Mucositis occurs anywhere mucosal tissues are found (Fig. 5.12). Mucositis of the esophagus, stomach, and intestines can cause bleeding and possible perforation of the lining of these structures. Infections are more likely in areas affected by mucositis because the mucosal barrier is compromised and normal intestinal flora can invade the tissues. Oral mucositis is very painful and will cause the patient to avoid eating. In addition, oral ulcers can become infected with oral bacteria. Several options are available

FIGURE 5.12. Mucositis. Painful oral ulcerations associated with radiation therapy. (Courtesy of Dr. Mike Brennan.)

to help alleviate pain and make eating more comfortable because an adequate diet is essential for positive therapeutic outcomes. Refer to Clinical Protocol #13 for treatment options for mucositis.

Radiation permanently destroys both the acinar and mucus-producing cells of the salivary glands that are in the field of radiation. The acinar cells are the first to be destroyed, resulting in the production of very thick, viscous saliva that does not have all of the properties it needs to properly protect the oral structures. Continued radiation will also destroy the mucus-producing cells. Both of these together or alone will result in xerostomia. Xerostomia will result in varying degrees of oral discomfort, taste perversions, an increased risk of caries, and difficulty eating, speaking, and wearing prosthetic appliances. Caries associated with xerostomia caused by radiation are called **radiation caries**. Radiation caries first occur around the cervical one-third of the teeth and result from an accumulation of acidogenic bacteria, a decrease in the amount of IgA in the saliva, and an impaired natural cleansing mechanism within the oral cavity (Fig. 5.13). The destruction of

FIGURE 5.13. Radiation caries. Caries caused by acidogenic bacteria and xerostomia induced by radiation therapy. (Courtesy of Dr. Carolyn Bentley.)

the salivary glands in radiation therapy is permanent, and patients must continue to deal with the complications of xerostomia for the rest of their lives. Oral complications due to radiation therapy can be controlled and the natural dentition can be maintained if the patient is compliant with a rigorous regimen of fluoride, meticulous homecare, and frequent professional care. Refer to Clinical Protocol #4 for suggestions to help patients with radiation-induced xerostomia.

Radiation therapy involving blood-forming bone marrow will cause **bone marrow suppression,** resulting in a decrease in white blood cells **(leukopenia),** red blood cells **(anemia),** and platelets **(thrombocytopenia)**. A decrease in white blood cells increases the patient's risk of acquiring infection. A low red blood cell count results in anemia and fatigue, shortness of breath, and increased demands on the heart and lungs. A decrease in platelets leaves the patient at risk for uncontrolled bleeding. Drugs are available to help increase the number of white and red blood cells produced to help lower the risk of infection and decrease fatigue. All patients undergoing radiation therapy have their blood tested routinely for early detection of these deficiencies.

Side effects associated with chemotherapy include most of the same side effects associated with radiation except they occur in the whole body and not just in the area of the radiation beam. Bone marrow suppression is a side effect of almost all chemotherapeutic agents. The potential for severe depletion of all the different blood cells is high. Therefore, patients have frequent blood tests and are monitored very closely for any symptoms associated with deficiencies. Oral and gastrointestinal mucositis occurs with many chemotherapeutic agents. Nausea and vomiting are almost always expected, and several drugs are available to help counteract this side effect. Severe xerostomia is often a complaint and will cause the same problems as xerostomia associated with radiation therapy; however, chemotherapy-induced xerostomia will resolve after completion of the therapy. Caries associated with chemotherapy are called **chemocaries**, and the same preventive measures used for radiation caries can be used to control chemocaries. Most chemotherapy patients will undergo temporary **alopecia**, or hair loss, starting within the first 2 to 3 weeks of treatment.

Prevention

Cancer does not have one cause, nor is the risk of getting cancer the same for every individual. Many of the risk factors for cancer are genetic, and many are determined by sex, age, and ethnicity. No one can change these factors. However, some of the risk factors for cancer are modifiable, and each person has the power to decrease or eliminate his or her cancer risk due to these factors. Cancer prevention is not a new concept. For example, tobacco cessation is the most effective way for individuals to eliminate or decrease their risk of developing many cancers. Refer to Box 5.5 for examples of behaviors that may decrease an individual's risk of developing cancer if modified.

BOX 5.5 Cancer Prevention Strategies

- Stop the use of tobacco products
- Proper nutrition
  - Eat a variety of fruits and vegetables every day
  - Reduce the amount of refined grains and sugars consumed
  - Reduce the amount of high-fat red meat consumed
- Maintain a healthy weight throughout life
  - Stay physically active
- Limit alcohol consumption
- Limit sun exposure and use sunscreen or other forms of protection
- Vaccinate against the human papilloma virus (HPV)

Common Cancers

This chapter concludes with a brief description of the most common cancers reported by the American Cancer Society. They include skin (squamous cell and basal cell), melanoma, lung, breast, prostate, and colorectal cancers. Metastatic cancer found in the oral cavity is also discussed. It is hoped that this information will increase the awareness of the dental hygienist about diseases not seen specifically in the oral cavity and that it will aid in patient management. All other oral cancers are discussed in the chapters pertaining to the specific clinical characteristics of the oral lesions. Table 5.4 lists the major forms of oral cancer, the appearance of their characteristic oral lesions, and the chapter in which they are discussed.

There are three major forms of skin cancer: BCC, SCC, and malignant melanoma. Each of these can be visible during the intra- and extraoral examination performed by the dental hygienist. Premalignant sun damage, as well as other visible skin abnormalities, should be brought to the attention of the patient. Any suspicious lesions should be referred for definitive diagnosis by a physician. Clinical Protocol #10 contains suggestions for advising patients about protecting the skin from ultraviolet radiation.

TABLE 5.4 Chapter Locations for the Major Types of Oral Cancers

Type of Cancer	Characteristic Lesion	Chapter
Squamous cell carcinoma (SCC)	Ulcers and a variety of other presentations	Chapter 12
Verrucous carcinoma	Raised, rough	Chapter 16
Melanoma	Pigmented	Chapter 15
Mucoepidermoid carcinoma	Soft tissue mass	Chapter 17
Lymphoma	Soft tissue mass and a variety of other presentations	Chapter 9
Ameloblastoma	Bone enlargement	Chapter 18
Kaposi sarcoma	Red/purple, raised/flat	Chapter 22

NAME: Basal cell carcinoma (BCC)

Etiology: Risk factors associated with BCC include exposure to ultraviolet light, genetic factors, and arsenic ingestion. A latency period of 20 to 50 years between the time of ultraviolet damage and the development of BCC is typical, emphasizing the need for protection during childhood and adolescence (Bader et al., 2011).

Method of Transmission: A genetic predisposition for BCC as seen in several syndromes, such as nevoid basal cell carcinoma syndrome (Chapter 20), may be transmitted to offspring.

Epidemiology: BCCs are not reportable for cancer statistics; however, the American Cancer Society estimates over 3.5 million cases of BCC and SCC of the skin are diagnosed each year (ACS, 2012a). BCC is the most common skin cancer and accounts for about 75 to 80% of these cases. BCC occurs more frequently in those between 55 and 75 years of age and occurs two times more often in men than in women (Bader et al., 2011). Statistics show an increase in patients younger than 35 years (Bader et al., 2011).

Pathogenesis: BCC starts in the cells of the basal (deep) layer of the epidermis in sun exposed areas. BCC will occur in any area in persons afflicted with nevoid BCC syndrome (see Chapter 20) and xeroderma pigmentosum. Xeroderma pigmentosum is an inherited disease in which the person lacks a specific enzyme necessary to repair sun-damaged DNA (Huether & McCance, 2004). BCC enlarges slowly, invades the surrounding tissues, and is locally destructive. In rare cases, untreated locally advanced BCC may also metastasize (Berlin et al., 2002; Von Hoff et al., 2009).

Extraoral Characteristics: Seventy percent of BCC are found on the head with most of these on the face (Bader et al., 2011). Early BCC presents as a papular growth with a sessile base. As the tumor becomes more nodular in size, features specific to BCC begin to appear. The central area of the nodule becomes depressed, ulcerated, and may become crusted. The borders of the lesion are raised and exhibit a pearly appearance, with a network of small capillaries visible on the surface. The lesions are painless and may have been present for varying lengths of time, depending on the size of the lesion. These tumors are locally destructive and can cause deformities if not treated early (Fig. 5.14).

Perioral and Intraoral Characteristics: BCC rarely appears intraorally. It may appear on the lips or vermilion border where it will have the same characteristic features noted above (Fig. 5.15).

Distinguishing Characteristics: The appearance of this tumor—the raised pearly borders with a visible capillary network surrounding a central depressed, crusted area—is its most distinguishing feature.

FIGURE 5.14. Basal cell carcinoma (BCC). A neglected BCC of the skin overlying the nose has ulcerated and invaded the deeper tissues. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

Significant Microscopic Features: Not applicable

Dental Implications: When a lesion with the characteristic features of BCC is observed, the patient should be referred to an appropriate physician for evaluation.

Differential Diagnosis: The following are considerations:

1. Actinic keratosis–Chapter 14. This lesion is also caused by sun damage. However, it presents as a plaque or patch of rough scaly skin that appears in a range of colors from yellow to brown or red. Lesions of actinic keratosis do not have rolled pearly borders with visible capillary networks. Advanced actinic keratosis may have a depressed central region, but would still not have the characteristic borders of BCC.
2. Keratoacanthoma–Chapter 16. Keratoacanthoma occurs on the sun-exposed skin. It begins as a small red papule that enlarges rapidly over 3 to 6 weeks into a 2- to 3-cm nodule. The rapid development of this lesion along with differences in its appearance differentiates it from BCC.
3. Seborrheic keratosis–Chapter 23. Seborrheic keratosis presents in older patients and appears clinically as a scaly brown-to-black plaque with well-defined margins. The lesion looks pasted on and usually has a greasy-feeling crust that can be rubbed off. Seborrheic keratosis does not present with rolled pearly margins that have a visible capillary network like BCC, and BCC does not present with a greasy feeling crust.
4. Squamous cell carcinoma–this chapter. SCC of the skin usually occurs on sun-damaged areas. Its early presentation may mimic that of BCC, but it will become ulcerated and scab over as it enlarges. Biopsy is the only way to definitively differentiate between the two.

FIGURE 5.15. Basal cell carcinoma (BCC). This tumor on the vermilion border exhibits typical rolled pearly borders with visible capillaries and central ulceration. (From Rubin E, Farber JL. Pathology. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2005.)

Treatment and Prognosis: Treatment options for BCC include surgical excision, laser surgery, cryosurgery (freezing with liquid nitrogen), electrodesiccation (burning), and radiation therapy. Radiation therapy can be used successfully for large tumors, those that involve areas that are difficult to access, or those that present other surgical problems such as tumors on the eyelids. The earlier these cancers are identified, the less invasive the procedures will have to be. The 5-year survival rate for localized BCC is over 99%. The median survival time for someone with metastatic BCC is 8 months. Patients who have had one skin cancer have a 50% chance of developing another BCC at a different site within 5 years. Patients should be monitored for new lesions on an annual basis for life.

NAME: Squamous cell carcinoma (SCC)

Etiology: Risk factors for SCC include ultraviolet light, arsenic ingestion, radiation therapy, areas that were previously burned, genetics, and skin diseases or injuries that cause scarring. In addition, both EBV and the HPV have been associated with SCC in the head and neck area.

Method of Transmission: SCC associated with EBV and HPV viruses occurs only after infection with the virus; otherwise SCC is not transmissible.

Epidemiology: SCCs are not reportable for cancer statistics; however, the American Cancer Society estimates over 3.5 million cases of BCC and SCC of the skin are diagnosed every year (ACS, 2012a). SCC accounts for about 20% of these cases (ACS, 2012a). SCC is found most often in fair-skinned older individuals with a history of sun damage to their skin. People living in the sun belt of the United States have a higher risk than those living in areas where the sun's rays are not so intense.

Pathogenesis: SCC begins in the **keratinocytes** of the outer epidermis, usually in areas of sun-damaged skin. It has an affinity for occurring in lesions of actinic keratosis and in scar tissue caused by burns and some skin diseases, such as discoid lupus erythematosus (see Chapter 12). Mutations in tumor-suppressor gene function caused by ultraviolet light are commonly seen in SCCs (Kumar et al., 2007). SCC, like BCC, has a defined in situ stage that may last for many years, increasing the opportunity for early diagnosis. Untreated SCC metastasizes in about 2% of cases.

Extraoral Characteristics: SCC often develops in a preexisting actinic keratosis. Early SCC often presents as a painless, nonhealing, rough, erythematic, scaly papule that may cause pruritus or itching. The lesion enlarges as it becomes indurated because of increased endophytic and exophytic growth. Eventually the surface becomes ulcerated, crusted, and bleeds easily. The surrounding tissues are usually erythematic and inflamed (Fig. 5.16). SCC may not present with these common features. It may look like many nonpathogenic entities or may actually develop within an area affected by another type of lesion. Any area that does not respond to appropriate treatment or does not heal or resolve within a specified time should be biopsied. SCC is as locally destructive as BCC, but because it metastasizes more readily, it is a more dangerous tumor.

Perioral and Intraoral Characteristics: Perioral lesions of the lip and surrounding area appear the same as described above (Fig. 5.17). Intraoral SCCs are common and are discussed in detail in Chapter 12.

Distinguishing Characteristics: Because there is such a range of possible presentations of SCC, any nonhealing lesion should be biopsied and identified.

Dental Implications: Lesions presenting as painless, nonhealing ulcers should be suspected as being SCC and should be biopsied.

FIGURE 5.16. Squamous cell carcinoma (SCC). Note the exophytic growth and ulceration this SCC exhibits and the increased vascular supply to the tumor visible in the surrounding area. (From Weber J, Kelley J. Health assessment in nursing. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

FIGURE 5.17. Squamous cell carcinoma (SCC). SCC presenting as a nodular ulceration of the lip. (From Goodheart HP. Goodheart's photoguide of common skin disorders. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

Differential Diagnosis:

1. Actinic keratosis–Chapter 14. Since SCC often develops in a preexisting lesion of actinic keratosis, these lesions should be evaluated by a physician or dermatologist.
2. Psoriasis and eczema–Chapter 23. SCC that develops in a person with psoriasis or eczema has often been mistaken for the lesions of these skin diseases. Any lesions from these skin disorders that do not respond to appropriate treatment should be biopsied.
3. Basal cell carcinoma–this chapter. SCC, in its early stages, often looks like BCC, but as SCC grows, the lack of rolled pearly borders with the visible capillary network should differentiate between the two.

Treatment and Prognosis: Treatment options for SCC include surgical excision, laser surgery, cryosurgery (freezing with liquid nitrogen), electrodesiccation (burning), radiation therapy, and PDT. The earlier these cancers are identified, the less invasive the procedures need to be. Radiation therapy can be used successfully for small tumors. It can also delay the growth of large tumors or those that involve areas on which surgery is difficult to perform. Chemotherapy can be used to treat SCC that has metastasized. The 5-year survival rate for localized SCC is over 95%. If the tumor metastasizes, the 5-year survival rate drops to 25% (Singh et al., 2000). Because patients who have had one skin cancer are at a higher risk for another for the rest of their lives, they should be monitored for new lesions on an annual basis.

NAME: Melanoma

Etiology: Refer to Box 5.6 for a summary of the risk factors associated with melanoma.

Method of Transmission: Melanoma may be associated with a slight genetic predisposition.

Epidemiology: Less than 5% of all skin cancers are melanomas; however, melanoma causes the most deaths due to

BOX **5.6** **Risk Factors Associated with Melanoma**

Factor	Details
Artificial tanning	Tanning beds, tanning parlors, sun lamps, and recreational exposure all increase the risk for melanoma
Nevi/Moles	A history of dysplastic nevi and/or having a large number of nevi put an individual at a higher risk for melanoma
Immunosuppression	Individuals who have compromised immune systems and those taking medications that decrease the immune response are at increased risk
Personal history of skin cancer	Those who have had one melanoma have a greater risk of developing another. Those with a history of basal cell or squamous cell skin cancers also have a higher risk of melanoma
Familial history of melanoma	Even though there is not a strong hereditary association, 10% of cases exhibit defects in two genes, CDKN2A and CDK4, which puts individuals with a family history of melanoma at a higher risk
Ultraviolet radiation	Individuals who work in the sun and/or live in areas that have intense sunlight and those that use tanning beds are at a higher risk for melanoma
Individual characteristics	Fair skin, light hair, blue eyes, and freckles increase an individual's risk up to two to three times
Sun exposure and previous sunburns	Ultraviolet A and B radiation both play a role in melanoma development. Risk of melanoma increases as the number of severe blistering sunburns that have occurred increases; especially problematic are sunburns that occur at a young age

skin cancer. It is the fastest-growing cancer in the United States and worldwide (MRF, 2011). The American Cancer Society estimates that 76,250 new cases of melanoma will be diagnosed in the United States in 2012 (ACS, 2012b). Most of these will be in the over 40-year-old age group. However, melanoma is one of the more common cancers in people younger than 30 (ACS, 2012b), and it has increased 50% in young women since 1980 (MRF, 2011). The rate of melanoma development is 10 times higher in whites than in blacks. Melanoma is most often found on the sun-exposed areas of whites and on non–sun-exposed areas such as the palms and soles of the feet in blacks (ACS, 2012b).

Pathogenesis: Melanoma develops within the melanocytes located deep in the basal layer of the **epidermis** (Fig 5.18) or in a preexisting **benign nevus**, which occurs in approximately 30% of cases. Oral melanoma is rarely encountered but should always be an element of the differential diagnosis for an unknown pigmented oral lesion. Normal melanocytic activity (tanning) is an innate defense mechanism against ultraviolet radiation damage to nuclear material (DNA) in the skin cells. When changes occur within the genetic material of the melanocytes, unsuppressed growth of abnormal melanocytes may take place. The growth is initially confined to the epidermis by the basement membrane but will breach the basement membrane eventually. How soon this process occurs depends on the type of melanoma developing. Of the three major types, two (superficial spreading and lentigo maligna) have relatively lengthy stages of horizontal growth where the tumor spreads out in all directions but remains within the confines of the basement membrane or in situ for up to several years before beginning vertical growth into the deeper tissues of the dermis. The third type (nodular) shows only vertical growth in the initial presentation and throughout the development of the lesion. Nodular melanoma, therefore, has a worse prognosis than the other types of melanoma. Vertical growth breaches the basement membrane, allowing tumor cells to spread to the regional lymph nodes via the lymphatic system. Distant metastases may occur through either the lymphatic or circulatory systems and may present in any area of the body (Fig. 5.19).

Extraoral Characteristics: Melanomas may present with a wide range of clinical characteristics, and many mimic the characteristics of benign pigmented lesions such as the nevus. The superficial spreading melanoma presents

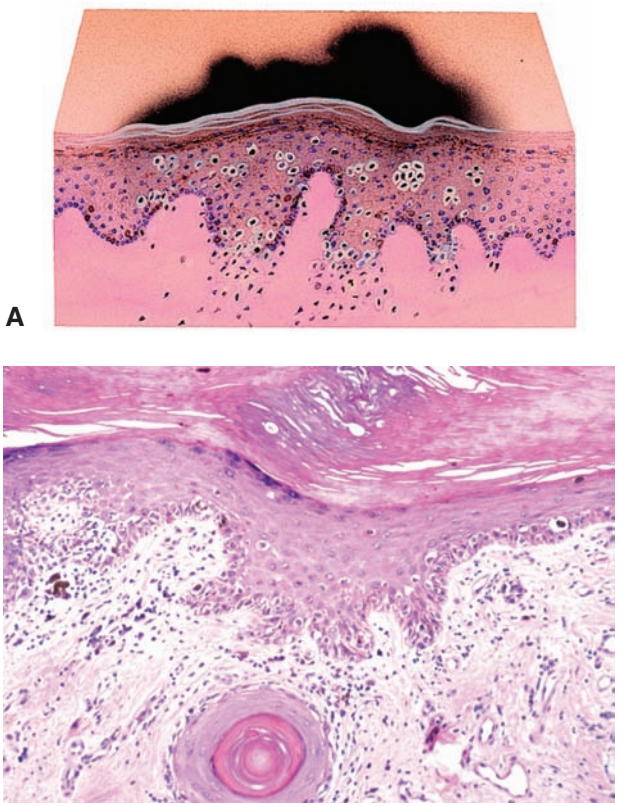


FIGURE 5.18. Melanoma. **A.** Melanoma develops from melanocytes found in the basal layer of the epidermis. (Provided by Anatomical Chart Co.) **B.** Malignant melanoma. Atypical melanocytes are present along the dermal-epidermal junction, with focal upward growth. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

FIGURE 5.19. Metastatic malignant melanoma. Note the multiple metastatic nodules on this patient's leg. (From Goodheart HP. Goodheart's photoguide of common skin disorders. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

as a variably colored nevus with a slightly raised irregular border in its radial phase. When it enters the vertical phase, the lesion will start to exhibit a nodular appearance and form raised variably colored, dome-shaped areas within the original lesion (Fig. 5.20). The lentigo maligna melanoma develops within sun-exposed skin and grows slowly over 20 or more years to a large size, often more than 5 cm. The associated melanoma presents as a large, flat, multicolored macule (Fig. 5.21A and B). Nodular melanoma will form firm dome-shaped, shiny, blue-black lesions (Fig. 5.22).

FIGURE 5.20. Melanoma. Clinically, the radial growth phase in malignant melanoma of the superficial spreading type is represented by the relatively flat, dark, brown-black portion of the tumor. There are three areas in this lesion that are characteristic of the vertical growth phase. All are nodular in configuration; two have a pink coloration, and the largest is rich, ebony black. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

A

B

FIGURE 5.21. A and B. Lentigo maligna melanoma. The radial growth phase of lentigo maligna melanoma is shown in these pictures. (A: From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.) (B: Courtesy of the Skin Cancer Foundation).

Perioral and Intraoral Characteristics: Perioral melanomas will exhibit the same characteristics as those described above. Intraoral lesions are described in Chapter 15.

Distinguishing Characteristics: The American Cancer Society has developed an ABCD rule to aid professionals and the general public in identifying suspicious lesions (ACS, 2012b). See Box 5.7 for an explanation of this rule. If any of the characteristics of a suspicious lesion are similar to those described by the ABCD rule, the lesion should be evaluated by a physician. The American Academy of Dermatology has added an additional letter to the ACS rule, E—for evolving or changing (AAD, 2011). Lesions that exhibit some sort of change in color, size, shape, texture, consistency, or feeling

FIGURE 5.22. Nodular melanoma. This nodule is surrounded with satellite lesions representing local metastasis. (From Goodheart HP. Goodheart's photoguide of common skin disorders. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

should be evaluated by a professional as soon as possible. Patients should be made aware of these characteristics to empower them to monitor their own skin/nevi.

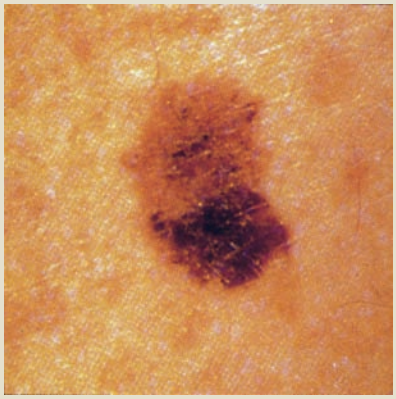
Significant Microscopic Features: Not applicable

Dental Implications: The clinician should observe all visible pigmented areas for the ABCDE rule and refer any suspicious areas for evaluation.

Differential Diagnosis: There are many different presentations of melanoma including nonpigmented and red melanomas. Any pigmented lesion with an unknown etiology should be biopsied.

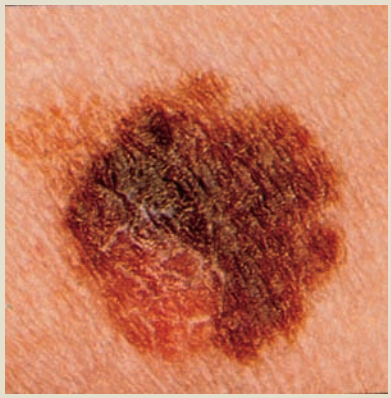
1. Benign nevus–Chapter 23. Melanoma can mimic a benign nevus. However, a benign nevus will rarely grow after it has reached its mature size, and the borders and colors of the nevus will stay uniform.
2. Kaposi sarcoma–Chapter 22. Kaposi sarcoma has a more purplish color because of its vascular origin, and there is probably a history of HIV infection or another condition that causes long-term immunosuppression.
3. Solar lentigo (liver spot)–Chapter 23. The solar lentigo is a hyperpigmented macule that develops on sun-exposed

BOX 5.7 **ABCDE Rule for Malignant Melanoma**

Picture	Rule
 A	Asymmetry One-half of the mole does not match the other half.
B	Border irregularity The edges of the mole are irregular, ragged, blurred, or notched.

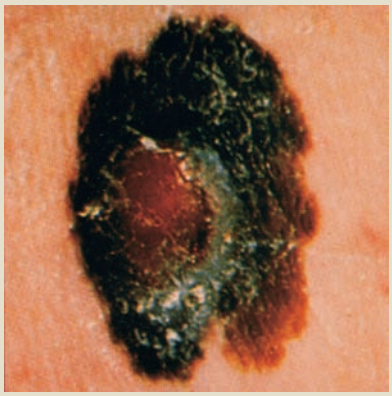
(continued)

BOX 5.7 ABCDE Rule for Malignant Melanoma *(continued)*



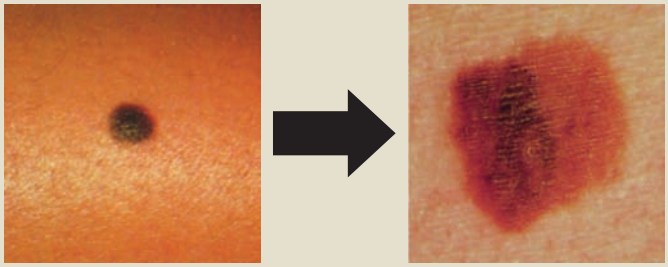
C

Color
The color over the mole is not the same. There may be differing shades of tan, brown, or black and sometimes patches of red, blue, or white.



D

Diameter
The mole is larger than 6 mm (about 1/4 inch or about the size of a pencil eraser), although in recent years, doctors are finding more melanomas between 3 and 6 mm.



E (1) (2)

Evolving
The mole (1) is exhibiting change behavior in appearance, sensation, or another characteristic (2).

Images from American Cancer Society. What you should know about melanoma. Dallas: American Cancer Society, 1995.

skin. They are usually larger than ephelides, or freckles, but unlike freckles do not fade when not exposed to the sun. Solar lentigines that develop darker pigmentation, thickening, or an irregular border should be evaluated for malignancy.

4. Tattoo (pigment introduced into the skin accidentally or by design for body decoration)–Chapter 15. The cause for any pigmented area should be determined. Intraoral pigmented lesions may be related to the accidental traumatic introduction of amalgam into the oral mucosa known as an amalgam tattoo.

Treatment and Prognosis: Although melanoma accounts for only 5% of skin cancers, it is responsible for the majority of deaths associated with skin cancer (ASCO, 2012). The prognosis associated with a particular melanoma depends on the thickness of the original, or primary, lesion and whether there has been metastasis to regional lymph nodes or distant metastasis. The thinner and more localized the tumor, the higher the chances of a complete cure. This is why it is so important to identify any suspicious lesion as early as possible. The 5-year survival rate for all melanomas combined is 91%. If the lesion is discovered in the early in

situ stage, the 5-year survival rate is 98%; if found in the regional lymph nodes or if distant metastasis has occurred, the 5 year survival rates are 62% and 15% respectively (ASCO, 2012). Surgery is the treatment of choice for all but the largest or most disseminated cases of melanoma. The smaller tumors are completely excised with a large margin of normal-appearing tissue. If the melanoma has spread to even one regional lymph node, all of the nodes in the region must be removed. Radiation therapy is used to increase the quality of life and prolong the life of patients who have advanced metastatic disease. Chemotherapy is used to prolong life and as an adjunct to surgery for tumors that have spread to lymph nodes. Neither radiation nor chemotherapy is used as the primary treatment for melanoma. Other promising treatments being researched and used at this time include targeted genetic therapy, immunotherapy and vaccines that help the immune system identify and destroy melanoma cells (ASCO, 2012).

Name: Breast cancer

Etiology: The etiology of breast cancer is mostly unknown. However, many factors that increase an individual's risk have been identified. Refer to Box 5.8 for a list of risk factors associated with breast cancer development.

Method of Transmission: A genetic predisposition for breast cancer may be inherited; otherwise breast cancer is not transmissible.

Epidemiology: The American Cancer Society estimates that approximately 226,870 women in the United States will be diagnosed with invasive breast cancer in 2012. An additional 63,300 women will be diagnosed with in situ breast cancer. Most of these women will be over the age of 50 (ASC, 2012c). A small number of men are also diagnosed with breast cancer every year. The American Cancer Society estimates that 2,190 men will be diagnosed with breast cancer in 2012 (ACS, 2012d).

Pathogenesis: Some 90% of breast cancers begin in the lobules that contain milk glands (lobular carcinoma) or in the ducts that carry the milk to the nipple (ductal carcinoma). Approximately 10% are less common variants of carcinoma, including inflammatory breast cancer and Paget disease of the nipple. Breast cancer probably results from two or three different events occurring throughout the life of the individual. The initial event may involve a change in the DNA structure of the breast cells and may occur very early in the life of the individual, even before the breast develops at puberty or prior to full breast maturity at the end of a successful pregnancy. The second and third events involve chromosomal changes such as defective functioning or loss of suppressor genes and/or the creation of oncogenes from proto-oncogenes. In addition, in approximately 70 to 80% of breast cancers, estrogen exposure is associated with the growth of the tumor. Most tumors occur in the upper outer quadrant of the breast and around the nipple. Local lymph node involvement usually begins with the axial nodes and may extend to the nodes located around the clavicle and the sternum. Common distant metastatic sites include the lungs, kidneys, liver, adrenal glands, ovaries, bones of the spine, ribs, pelvis, and skull, including the maxilla and the mandible.

Extraoral Characteristics: None, unless the clavicular lymph nodes are involved.

Perioral and Intraoral Characteristics: Metastatic breast cancer may present as radiolucent areas in the maxilla or mandible, which may or may not be associated with the roots of a tooth.

BOX 5.8 **Risk Factors Associated with Breast Cancer**

Factor	Details
Age	The risk of breast cancer increases with age
Race	More whites are affected than blacks, but more blacks die from the disease
Previous history of breast cancer	There is a three to four times greater risk of breast cancer in the opposite breast after having cancer diagnosed in one breast
Previous history of other hormone-associated cancers	Ovarian and endometrial cancer are examples of other hormone-associated cancers that increase the risk of having breast cancer
Family history of breast cancer	Breast cancer in one primary relative (mother, sister) increases risk; two or more relatives with breast cancer increases that risk even more
Genetic predisposition	Some 5–10% of breast cancers are known to be associated with the BRCA 1 and 2 genes
Estrogen and progesterone exposure	Early menstruation, late menopause, and the use of hormone replacement therapy increase a woman's overall exposure to estrogen; women who had their first pregnancy after age 35 or those who never had a full term pregnancy are also at increased risk
Lifestyle factors	Obesity, lack of physical activity, and more than one or two alcoholic drinks per day have all been associated with an increased risk of breast cancer
Radiation	High doses of ionizing radiation such as radiation therapy for other cancers that place the breast in the radiation beam increase the risk for breast cancer in that breast. The use of tanning beds and x-rays may also increase risk

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: These patients should be followed closely to determine the origins of any suspicious intraoral radiographic areas. Patients taking Tamoxifen or an aromatase inhibitor may present with exaggerated postmenopausal symptoms.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment depends on multiple factors including the stage of the disease, familial history, patient preferences, and type of cancer. Most in situ breast cancers are surgically removed during either a lumpectomy or simple mastectomy, removal of just the breast tissue and skin. Invasive or infiltrating cancers are treated with surgery and either chemotherapy, radiation therapy, or both. Often, large tumors are treated with chemotherapy to shrink the tumor prior to surgery. Patients who have estrogen-receptive tumors are usually placed on medication that inhibits the production of estrogen for from 5 to 10 years following completion of their therapy. Patients will take an antiestrogen such as Tamoxifen for 5 years followed by up to 5 years of an aromatase inhibitor or vice versa. Recent studies have shown significant reductions in the risk of recurrence when this therapy regimen is followed. The 5-year survival rate for cancer limited to the breast is 99%, 84% if it has spread to the regional lymph nodes and 23% if it has spread to distant sites (ACS, 2012c). It is estimated that about 39,510 women and 410 men in the United States will die from breast cancer in 2012 (ACS, 2012c; ACS, 2012d).

NAME: Prostate cancer

Etiology: The etiology of prostate cancer is unknown. The only recognized risk factors at this time are being over 65 years of age, having a family history of prostate cancer, and being of African descent.

Method of Transmission: Not applicable

Epidemiology: The American Cancer Society estimates that 241,740 new cases of prostate cancer will occur in 2012 (ACS, 2012). Black men have a significantly higher incidence than white men (ACS, 2012).

Pathogenesis: Most prostate tumors are adenocarcinomas or glandular tumors. Androgens such as testosterone are thought to play a significant role in the development of this cancer. There are no symptoms associated with prostate cancer in the early stages of the disease. More advanced cancers will obstruct the flow of urine from the bladder and cause difficulty in starting or stopping urine flow and in urinary frequency, especially at night. Early detection is the most important factor relative to survival with prostate cancer. Until recently, the American Cancer Society recommended most men have annual blood tests to detect prostate-specific antigen (PSA) and an annual digital rectal examination starting at age 50. Elevated levels of PSA in the blood are sometimes associated with progression of prostate cancer or a recurrence of prostate cancer. Men at high risk for prostate cancer were told to start these examinations earlier than age 50. In October of 2011, the US Preventive Services Task Force released draft recommendations against prostate screening examinations for most men (the recommendations may change after the time period for public comments is completed). This was based on a review of studies showing, among other findings, that screening had no statistically significant effect in preventing deaths from this cancer. The public and professional response to these recommendations was immediate. In light of the controversy surrounding the release of the draft recommendations, the ACS is recommending that men consult with their health care provider about whether to be screened for prostate cancer or not. The discussion should include information about the uncertainties, risks, and possible benefits of being screened (ACS, 2012e).

Extraoral Characteristics: None

Perioral and Intraoral Characteristics: None

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: These patients should be followed closely to determine the origins of any suspicious intraoral radiographic areas.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatments include surgery, radiation, chemotherapy, and hormonal therapy. Treatment can lead to temporary or permanent incontinence and varying degrees of sexual dysfunction. A cancer vaccine (Provenge) has recently become available for men with advanced, nonresponsive prostate cancer. Immune cells are removed from the man's body and exposed to the vaccine then returned to body where they attack the cancer cells (ACS, 2012). The prognosis for prostate cancer found in the early stages is 100% for 5-year survival, 98% for 10-year survival, and 91% for 15-year survival (ACS, 2012). Obesity and smoking have been associated with a higher risk of dying from prostate cancer the second leading cause of cancer death in men, with an estimated 28,170 deaths expected in 2011 (ACS, 2012).

NAME: Lung cancer

Etiology: Tobacco smoking is the most significant risk factor for developing lung cancer. Other significant risk factors include exposure to occupational or environmental secondhand smoke, radon, asbestos, arsenic, radiation, and air pollution (ACS, 2012).

Method of Transmission: While not transmissible in the classic sense, there appears to be a genetic predisposition or inherited susceptibility for lung cancer, especially in those who develop the disease at a young age (ACS, 2012).

Epidemiology: The American Cancer Society estimates 226,160 new cases of lung cancer will occur in 2012. The incidence rate has been declining in men since 1994 and has just started to decline in women after years of consistent increases (ACS, 2012).

Pathogenesis: Tobacco smoke and the associated carcinogens contained in the smoke are associated with 85 to 90% of lung cancers. The carcinogens cause mutations in chromosomes, creation of oncogenes, and defects in tumor-suppressor genes. A genetic predisposition is also a factor in the development of lung cancer. Loss of a specific tumor-suppressor gene (*p*53) has been determined in 50 to 80% of lung cancers (Rubin & Strayer, 2012). Most lung cancers manifest with clinical symptoms such as cough, sputum production, and difficult or painful breathing. These symptoms are associated with most common pulmonary conditions, and most individuals (especially smokers) tend to ignore them until they disrupt their everyday lives. Lung cancer begins in the tissues of the bronchial mucosa, breaches the basement membrane as it enlarges, and then spreads into the local tissues. Eventual metastasis to the brain, bone marrow, and liver is most likely.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: Not applicable

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Some 95% of primary lung or bronchiogenic cancers comprise four specific histologic types: SCC, large cell carcinoma, adenocarcinoma, and small cell carcinoma.

Dental Implications: Small cell carcinoma may present with symptoms similar to those of Cushing syndrome, in which there is excess production of hormones, specifically cortisol, by the adrenal glands. In lung cancer, these symptoms represent a paraneoplastic syndrome caused by the hypersecretion of adrenal hormones by the tumor cells, not the adrenal glands. This might be important in analyzing health history information and in possible explanations for intraoral and extraoral findings. Specifically, Cushing syndrome presents with muscle weakness, facial edema, hypertension, and increased pigmentation, often around the oral and perioral area. This information added to a history of smoking, chronic cough, and other symptoms might lead to a referral and early diagnosis. Cushing syndrome is discussed in Chapter 7. In addition, dental professionals have the opportunity to help decrease the incidence of lung cancer by providing tobacco cessation information and help during dental appointments. Studies have shown even brief interventions are effective in helping the individual decide to attempt to quit smoking. Tips for tobacco cessation and motivational interviewing are located in Clinical Protocols #24 and #27.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment options depend on the type of cancer and the stage at which it is diagnosed. Surgery, chemotherapy, and radiation therapy are all possible with combinations of two or more treatments often necessary. Like oral cancer, lung cancer has few if any early symptoms, and by the time symptoms are acknowledged, the disease has progressed to more advanced stages. The 1-year survival rate for lung cancer is about 43%; the 5-year survival rate for all stages combined is 16%. If discovered in the earliest stages, the 5-year survival rate is 52% (ACS, 2012). Lung cancer is the leading cause of cancer death in both men and women, with 160,340 deaths expected in 2012 (ACS, 2012).

NAME: Colorectal cancer

Etiology: Risk factors include increasing age, personal or family history of colorectal cancer, inflammatory bowel disease (IBD), smoking, physical inactivity, type 2 diabetes, and obesity, among others. In addition, individuals with colorectal polyps, especially those associated with certain genetic syndromes (for example, familial adenomatous polyposis [FAP] or Peutz-Jeghers syndrome) may have a significantly higher risk of this type of cancer than the general population.

Method of Transmission: Aside from the inherited syndromes, this cancer is not transmissible.

Epidemiology: The American Cancer Society estimates that approximately 143,460 new cases of colorectal cancer will be diagnosed in 2012. The highest rate is found in blacks. The number of men and that of women diagnosed with colorectal cancer are approximately the same. About 91% of colorectal cancers occur in people over the age of 50 (ACS, 2012).

Pathogenesis: Adenomatous **polyps** of the colon and rectum usually precede the development of colorectal cancers. Anything that is associated with the growth of these polyps will be associated with the development of colorectal cancers. It normally takes about 10 to 15 years for abnormal cells to grow into a polyp and then become cancerous. Routine screening after the age of 50 for those with no identified risk factors will help detect abnormal polyps before they can cause harm. Individuals with significant risk factors should discuss a screening schedule with their physician. The regular use of nonsteroidal anti-inflammatories, adequate exercise, and a diet rich in fruits and vegetables and low in red meats may decrease the risk of colorectal cancers.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: **Peutz-Jeghers syndrome** (see Chapter 10) is an inherited condition associated with an increased risk of intestinal polyps that have a slight potential for malignant transformation. Occasionally, these polyps can be found in the colon or rectum. One of the other presenting features of this syndrome is mucosal and perioral brown-pigmented macules, or ephelides. The hands and feet may also be affected by the macular pigmentations.

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: Oral and perioral melanotic macules in the presence of other historical information such as gastrointestinal problems might lead the clinician to suggest a referral for a definitive diagnosis and appropriate screening examinations.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Surgery is the most common treatment for colorectal cancer. The extent of surgery depends on the extent of the cancer. In situ cancer that is confined to a polyp can be treated by simple removal of the polyp. Cancer that has progressed might necessitate the removal of a portion of the colon or rectum and might require the removal of any involved lymph nodes. As a last resort in extensive disease the surgeon might have to perform a **colostomy** so that wastes can be passed through an opening in the abdomen into a bag. Chemotherapy and radiation therapy can be used in addition to surgical procedures. Recently, drugs that target the tumor's ability to create blood vessels have been used in cases where other treatments are no longer effective or in combination with chemotherapy or radiation therapy. The 5-year survival rate for cancer that is confined to the bowel wall is 90%, if it has spread to the lymph nodes it is 69%, and if it has metastasized to distant sites it is 12% (ACS, 2012). The American Cancer Society estimates 51,690 people will die of this disease in 2012.

NAME: Oral metastatic cancer

Etiology: Cancer of any type from any primary tumor may metastasize to the oral cavity. Breast, lung, prostate, renal cell, and colorectal cancers are the most likely to metastasize to the jaws (Regezi et al., 2008).

Method of Transmission: Not applicable

Epidemiology: No data available

Pathogenesis: Metastasis to the oral cavity is rare and usually occurs 2 to 3 years after the diagnosis of a primary tumor and completion of appropriate treatment. Metastasis to the mandible is more common than to the maxilla, and metastasis to either or both jaw bones is more common than to the oral soft tissues. Metastasis to the jaw bones may be the first sign of cancer in about 30% of cases (Regezi et al., 2008).

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: Lesions of the jaw bones can present as poorly defined radiolucent or, rarely, radiopaque defects that may or may not be associated with tooth roots (Fig. 5.23). The patient may experience pain, loosening of the teeth, bone expansion, or growth of a soft tissue tumor. Paresthesia or numbness of the lip or other soft tissue is common, along with an increased risk for pathologic fractures of the jaw.

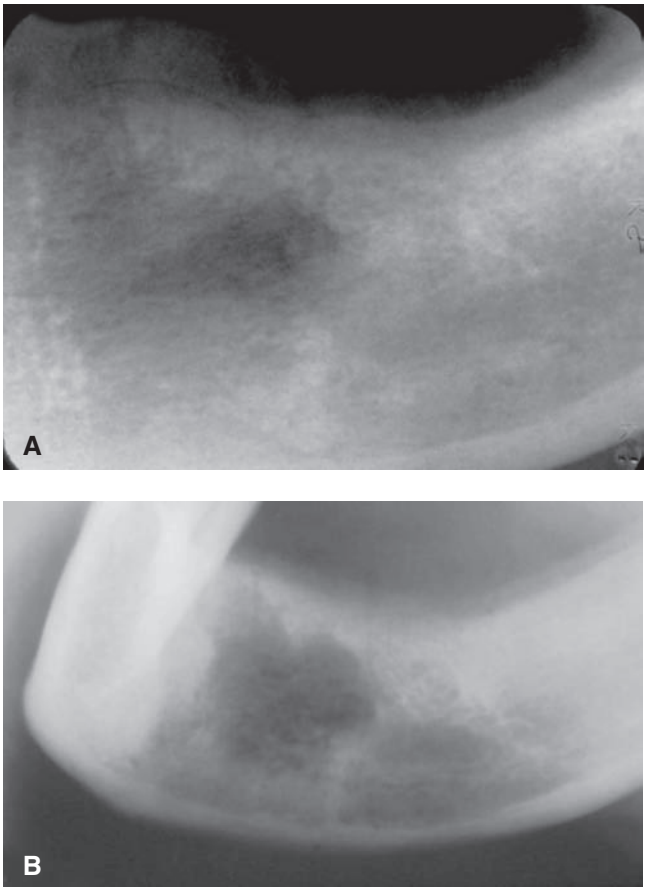


FIGURE 5.23. Metastatic cancer. Radiographs A and B show different views of the same radiolucent lesion with poorly defined margins representing a metastatic breast cancer. (Courtesy of Dr. Robert P. Langlais.)

Distinguishing Characteristics: The ill-defined border of the lesions is the most significant observation.

Significant Microscopic Features: Not applicable

Dental Implications: Patients who present with a history of cancer should always be examined for any suspicious areas in the oral cavity or on any periodic radiographic surveys.

Differential Diagnosis: The differential diagnosis of any of these findings would include primary oral cancer and any similar-appearing bone or oral lesions. Biopsy is necessary for a definitive diagnosis.

Treatment and Prognosis: Treatment for metastatic cancer in the oral cavity is determined by the type of primary tumor and the extent of metastasis. The prognosis for patients with this type of metastasis is very poor, with about 10% reaching 5 years (Regezi et al., 2008).

SUMMARY

- The three main categories of cells based on their ability to reproduce are labile, stable, and permanent cells. Each cell has a specific genetically determined growth potential.
- Some of the genes that control growth include proto-oncogenes, tumor-suppressor genes, and DNA repair genes. If a change or mutation occurs in any of these genetic control mechanisms, unregulated growth may occur.
- Genetic mutations initiate the neoplastic process and can cause defective functioning of the tumor-suppressor genes and the DNA repair genes, resulting in neoplastic growth.
- Proto-oncogenes can mutate and become oncogenes that also support uncontrolled growth of the affected cells.
- Genetic mutations can be inherited; they can be caused by chemical, environmental, or viral agents; or they can be associated with an immune system defect.
- Benign neoplasms grow locally and are usually encapsulated. They do not metastasize but can still cause death or disability, depending on the location of the tumor.
- Malignant tumors grow by extension into the surrounding tissues. They disrupt the nutrient supply to normal cells and destroy extracellular substances so that tissues in the area are weakened, and the tumor cells can penetrate more easily.
- An epithelial tumor that has not breached the basement membrane is called carcinoma in situ and is highly treatable.
- Cancer cells break off from the primary tumor and move deeper into the tissues, where they spread the disease through the lymphatic and blood vessels to distant sites, in a process called metastasis.
- Cancer can also spread to adjacent organs by movement of the cancer cells through the pleural and abdominal cavities in a process called seeding.
- Neoplasms may be suspected because of symptoms a patient reports or signs a health care professional observes. Neoplasms may also be detected by one of the many screening methods in use at this time.
- Definitive diagnosis is only made by microscopic examination of tumor cells obtained by excisional, incisional, or other form of biopsy.
- Benign cells are well differentiated and do not exhibit the structural changes that are seen in malignant cells. Malignant cells exhibit varying degrees of anaplasia, pleomorphism, hyperchromatic nuclei, and other features.
- Pathology reports also define the number of mitotic figures seen in the sample, indicating rapid growth. Other factors are determined during or after surgery or other tests. These factors include whether regional or distant lymph nodes are involved and whether there has been metastasis to a distant site.
- The cancer grading system classifies cells in grades I through IV according to their microscopic features. The higher the cancer grade, the more likely a tumor will be aggressive.
- Tumor staging appears to be more reliable in determining probable disease outcomes. Tumor staging systems, such as the TNM system, consider the size of the tumor and whether it involves the regional lymph nodes and/or has metastasized to a distant site.
- Paraneoplastic syndromes are not common but when present can include some or all of the following: fever of unknown origin, weight loss, anorexia, endocrine imbalances, anemia, blood clots, neurologic problems, fatigue, and pain.
- Surgery is a major form of cancer therapy and is often the initial therapy chosen unless the tumor is too large or is located in an inaccessible area.
- Radiation therapy may be used in conjunction with surgery and/or chemotherapy to help ensure that all cancer cells are eliminated if possible. Radiation affects rapidly dividing cells, which are especially radiosensitive, and either destroys them or destroys their ability to replicate.
- Chemotherapy works in a similar way but may not necessarily target just rapidly dividing cells.
- Hormone therapy can be useful when a tumor depends on a particular hormone for growth or when a tumor will not grow in the presence of a specific hormone.
- Immunotherapy is a relatively new area of treatment designed to enlist our own immune system to destroy the cancer cells and thus spare the body's normal cells.
- Cancer therapies have many associated side effects. Most of the side effects are temporary, but many can be permanent. Surgery can result in loss of function and form. Radiation therapy can cause irreversible damage to salivary glands, reproductive organs, and other structures. Radiation and chemotherapy cause temporary side effects, increasing an individual's risk of getting an infection, and can cause oral and gastrointestinal mucositis, caries, nausea, vomiting, and alopecia, among others.
- While many of the risk factors associated with cancer such as age, sex, and ethnicity are unchangeable, many others can be modified, and individuals have the power to decrease their risk of cancer associated with these factors.

CHAPTER REVIEW

Case Study 5.1

Study Figures 5.24 and 5.25 then respond to the questions below.

1. Write a clinical description of the lesions seen in these figures. The consistency for Figure 5.24 is fluctuant, and that of Figure 5.25 is indurated.

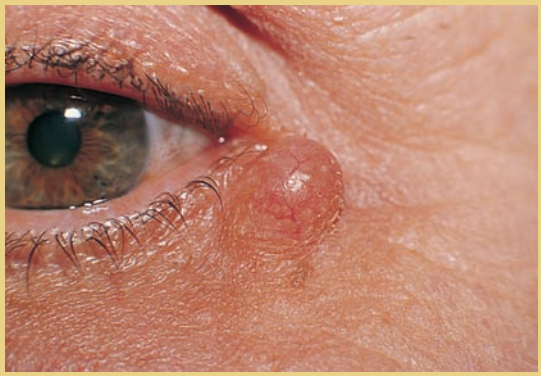


FIGURE 5.24. (From Tasman W, Jaeger E. The Wills Eye Hospital atlas of clinical ophthalmology. 2nd ed. Baltimore: Lippincott Williams & Wilkins, 2001.)

2. One of these is a common skin cancer. Pick the one that you think is the cancer and decide which type of skin cancer you think it is. What elements of the clinical description were the major factors in your decision?
3. Which of these would you want to refer for a biopsy?

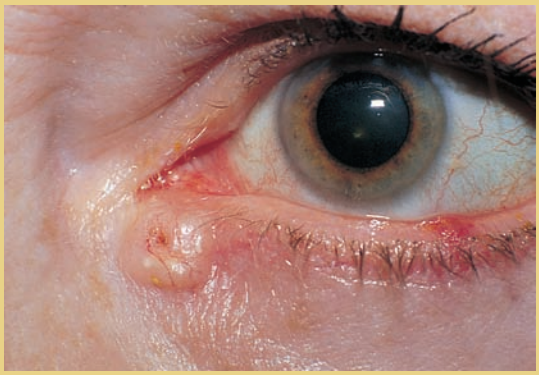


FIGURE 5.25. (From Tasman W, Jaeger E. The Wills Eye Hospital atlas of clinical ophthalmology. 2nd ed. Baltimore: Lippincott Williams & Wilkins, 2001.)

For answers and additional review activities, log in to **thePoint.lww.com**

Case Study 5.2

Study Figures 5.26 and 5.27 then respond to the questions below.

1. List the characteristics these lesions have in common.
2. One of these lesions is malignant. Which one?
3. In your opinion, what types of lesions are represented in these pictures?
4. What is the most common cause of the conditions seen in Figures 5.26 and 5.27?

FIGURE 5.26. (From Goodheart HP. Goodheart's photoguide of common skin disorders. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

5. You see both of these patients for routine dental hygiene care. What is your responsibility in these cases?
6. How will you suggest your patients prevent this type of lesion?

FIGURE 5.27. (From Moore KL, Dalley AF II. Clinical oriented anatomy. 4th ed. Baltimore: Lippincott Williams & Wilkins, 1999.)

For answers and additional review activities, log in to **thePoint.lww.com**

Critical Thinking Activities

1. You have completed an intraoral and extraoral examination on an elderly patient and have discovered the lesion depicted in Figure 5.28. Create responses to the following situations:

FIGURE 5.28. Lentigo maligna melanoma. Biopsy of this lesion demonstrated invasion into the dermis. (From Goodheart HP. Goodheart's photoguide of common skin disorders. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

   A. Mr. Nantz is a new patient who you do not know at all. Write a dialogue that will not only help you to get to know Mr. Nantz, but will also educate him about suspicious skin lesions and the importance of complying with a referral to a physician.
   B. Mr. Yarrington has been seen in your office every 3 to 4 months for the last 10 years. He is partially deaf, has poor eyesight, and is confined to a wheelchair. He prides himself on his ability to take public transportation to his medical/dental appointments and thus not be as much of a burden on his daughter, who works. This is the first time you have seen Mr. Yarrington in several years (he has been seen by other hygienists in your office). You have looked in his dental record and have found no mention of this obvious lesion. (1) What would be the best way to inform Mr. Yarrington about this suspicious lesion? (2) What can you do to make sure lesions like this are noted in the dental record and that appropriate follow-up procedures are used in the future?
2. This chapter has introduced many cancers not included in any area a dental hygienist might examine. How far do you think a dental professional can go with this knowledge? Can it be used to suggest patients of a certain age group be screened for prostate cancer, for example? Would you feel comfortable discussing risk factors for breast cancer with your female patients? Write down what you think you could incorporate into your practice of dental hygiene and how you would incorporate it. Share this with the rest of the class and enjoy a good exchange of opinion and ideas.
3. Read the Application 5.1, "Stem Cells: Science Fiction or Reality?" What impact will this have on the practice of dentistry in the future? What do you think the role of the dental professional should be in discussing stem cells and stem cell banking (tooth and cord blood) with patients?

Portfolio Activity

Make arrangements to visit a support group for cancer patients and/or survivors. Bring information about oral care during and after treatment, and be prepared to answer any questions the participants might have. Talk to the individuals and ask about their dental needs and possible oral side effects of treatment they are dealing with. Conduct evidence-based research to try to help with their problems, then revisit with them and discuss what you have discovered. Write a short description for your portfolio of your experience, what you think you have learned from the experience, and the individuals with whom you have interacted. How will this experience prepare you for the practice of dental hygiene?

Media Menu

Web Sites

American Society of Clinical Oncology: Oncologist-approved cancer information
http://www.cancer.net/portal/site/patient

American Academy of Dermatology: PDF "Body Mole Map" (under "Skin Examinations")
http://www.skincarephysicians.com/skincancernet/whatis.html

Multimedia Resources

Cancerquest: Emory/Winship Cancer Institute—Excellent video explaining the development of cancer with animations
http://www.cancerquest.org/cancer-biology-animations.html#

Microscope Imaging Station: Cancer Cells Behaving Badly—Very interesting video presentation with narration
http://youtu.be/JYXaF7ZJii8

Study Tools

Take advantage of additional online resources to help you study and ace your exams!

- Answers to case studies in the book
- Additional case studies and answers
- Interactive quiz bank with answer feedback
- Fully searchable e-book for quick lookup and studying on-the-go
- Expanded Media Menu with direct links to related Web sites and multimedia resources
- Supplemental references

thePoint Online resources and links are available at http://thepoint.lww.com/DeLong2e.

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CHAPTER 5 **LESION/CONDITION SUMMARY TABLE**

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Basal Cell Carcinoma (BCC)	Ultraviolet light, genetic syndromes (i.e., nevoid basal cell carcinoma syndrome, xeroderma pigmentosum)	Slow-growing, locally invasive, very slight chance of metastasis	Nodular growth with a depressed, ulcerated, or crusted central region surrounded by raised pearly borders that have visible capillaries on their surface; 70% found in the head and neck area	Not applicable	Surgical excision, laser surgery, cryosurgery, electrodesiccation, and radiation therapy	Note suspicious lesions during the head and neck examination and refer to the physician for evaluation; not found on intraoral surfaces
Squamous Cell Carcinoma (SCC)	Ultraviolet light, ionization radiation, genetic factors, Epstein-Barr virus (EBV), human papillomavirus (HPV), skin diseases	May start in actinic keratosis or other damaged skin, locally destructive, high potential for metastasis	Painless, nonhealing lesion (ulcer, leukoplakia, erythroplakia, etc.), pruritic, surrounding area red and vascular	Not applicable	Surgical excision, laser surgery, cryosurgery, electrodesiccation, radiation therapy, and photodynamic therapy (PDT)	Intra- or extraoral lesions presenting as painless, nonhealing ulcers or other nonresolving lesions should be suspected as being squamous cell carcinoma (SCC) and should be biopsied.
Melanoma	Ultraviolet light, dysplastic nevi, HX of skin cancer, fair skin, light hair, freckles, genetic factors	Starts in melanocytes in basal layer or in nevi, most spread superficially before invading the deeper tissues and metastasizing, nodular invades immediately, high rate of metastasis	Melanomas may be brown, black, red, or unpigmented; intraoral uncommon	Not applicable	Surgical excision including a wide margin of normal tissue is the primary treatment, with radiation and chemotherapies used to prolong life and improve quality of life for as long as possible	Follow ABCDE rule to identify suspicious pigmented lesions, refer suspect lesions for evaluation.
Breast Cancer	Age, genetic factors, family HX, previous HX of hormone-associated cancers, estrogen/ progesterone exposure, lifestyle factors, radiation	Most often starts in the milk glands or the ducts that carry milk, usually a combination of events initiates growth; may be localized for extended period before invading local tissues; lymph nodes and eventually metastasizing to lungs or bone, etc.	Usually appear in upper outer quadrant as firm lump fixed to underlying tissues, may feel supraclavicular nodes if involved	Not applicable	Lumpectomy/ mastectomy primary treatment, chemotherapy and radiation are often cotherapies	Thoroughly examine these patients for any sign of an oral metastatic lesion; tamoxifen or aromatase inhibitor may present exaggerated postmenopausal symptoms
Prostate Cancer	Age over 65 and family HX	Glandular tumor, slowly progressive, frequently recurs	Few if any symptoms in early stages, urinary obstruction, frequency and difficulty starting or stopping flow in later stages	Not applicable	Surgery, radiation, chemotherapy, and hormonal therapy	Thoroughly examine these patients for any sign of an oral metastatic lesion; mention prostate-specific antigen (PSA) biomarker testing done for screening to patients

continues

CHAPTER 5 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Lung Cancer	Tobacco smoking is the most common cause of lung cancer, genetic factors.	Carcinogens cause mutations in DNA initiating neoplastic growth; starts in bronchial mucosa and then spreads through the basement membrane to invade local tissues; metastasis to bone most likely	Leading cause of death in men and women; symptoms such as cough, sputum production, and difficult or painful breathing; most individuals (especially smokers) ignore until cancer is advanced.	Not applicable	Treatment options depend on the type of cancer and stage at diagnosis; surgery, chemotherapy, radiation therapy all possible with combinations of treatments often necessary	Any type of tobacco cessation intervention (even brief intervention) may help patients decide to quit
Colorectal Cancer	Age, family HX of colorectal cancer, inflammatory bowel disease (IBD), smoking, physical inactivity, type 2 diabetes, obesity, etc.	Associated with polyps that form in the colon and rectum	No observable signs unless associated with a syndrome like Peutz-Jeghers	Not applicable	Surgery is primary therapy with radiation and chemotherapies added if necessary to prolong life, etc.	Oral and perioral melanotic macules may indicate Peutz-Jeghers syndrome, which is associated with this type of polyp. Any patient who exhibits this type of oral and/or perioral pigmentation should be referred for medical evaluation.
Oral Metastatic Cancer	Any type of cancer but most frequently breast, lung, prostate, renal cell, and colorectal	Usually occurs 2–3 y after diagnosis of a primary tumor; may be the first sign of cancer in about 30%	Metastasis to mandible more common than maxilla, soft tissue least common, metastatic lesion may present as poorly defined radiolucent areas or, less commonly, radiopaque lesions	Not applicable	Treatment determined by the type of primary tumor and extent of metastasis; prognosis is very poor, with about 10% reaching 5 y.	Any patient with a history of cancer should be thoroughly examined, with any nonhealing or suspicious lesions being referred quickly for evaluation.

CHAPTER 6

Developmental, Genetic, and Congenital Disorders

KEY TERMS

Allele	Hypertelorism
Aneuploid	Hypodontia
Anodontia	Hypotelorism
Autosomal	Inherited
Barr body	Intermediate expression
Bossing	Inversion
Carrier	Karyotype
Centromere	Locus
Chromatin	Macroglossia
Chromatid	Monosomy
Chromosome	Morphogenesis
Codominance	Mosaicism
Congenital	Multifactorial inheritance
Deletion	Nondisjunction
Developmental abnormality	Penetrance
Diploid	Periosteum
Dominant	Phenotype
Epicanthal fold	Photophobia
Euploid	Prognathism
Expressivity	Pseudoanodontia
Fetus	Recessive
Gamete	Somatic
Gene	Telomere
Genome	Teratogen
Genotype	Teratology
Haploid	Trait
Heterozygous	Translocation
Homologous	Trisomy
Homozygous	Xerophthalmia
Hyperhidrosis	Zygote

LEARNING OUTCOMES

1. Define and use the key terms in this chapter.
2. Compare and contrast the terms developmental, genetic, and congenital.
3. Provide examples of teratogenic agents and describe how a teratogenic agent may affect morphogenesis.
4. Describe the inheritance pattern of autosomal dominant disorders and of autosomal recessive disorders.
5. Describe the inheritance pattern of X-linked disorders.
6. Discuss the concept of multifactorial inheritance.
7. State the etiology, method of transmission, and pathogenesis of the disorders discussed in this chapter.
8. Describe the characteristics of developmental, genetic, and congenital disorders.
9. Describe the dental implications and appropriate dental treatment modifications associated with the disorders discussed.

CHAPTER OUTLINE

Concepts of Developmental Abnormalities
Developmental Abnormalities
Fetal alcohol spectrum defects
TORCH syndrome
Overview of Genetic Concepts
Chromosomes
Sex Chromosomes
X Chromosome Inactivation
Genes
Elements of Genetics
Genetic Disorders
Abnormal Number of Chromosomes
Abnormalities in Chromosome Structure
Mosaicism
Trisomy 21
Klinefelter syndrome
Turner syndrome
Single-Gene or Mendelian Disorders
Marfan syndrome
Cleidocranial dysplasia
Treacher Collins syndrome
Ehlers-Danlos syndrome
Papillon-Lefèvre syndrome
Gingival fibromatosis
Ectodermal dysplasia
Multifactorial Inheritance
Cleft lip and/or palate

RELATED CLINICAL PROTOCOLS

#16 Oral Health Care Management for the Patient with Diabetes
#17 Oral Health Care Management for the Patient with Heart Disease
#21 Oral Health Care Management for the Patient on Antithrombotic Therapy

The terms "developmental," "genetic," and "congenital" are often used incorrectly. **Developmental abnormalities** occur when there is a disturbance in the development of the body that results in an abnormality. The developmental abnormality can be very severe and cause spontaneous abortion or miscarriage or it can be very minor and cause few, if any, problems. Genetic conditions involve a change in the DNA or chromosomes of an individual and can be inherited, passed from generation to generation, or may occur spontaneously. Spontaneous genetic damage will only be passed to future generations if the gametes (egg and sperm) are affected. Many genetic conditions are not compatible with life and result in a spontaneous abortion or early infant death; others can be very mild and not noticed. **Congenital** abnormalities, sometimes called birth defects, are present at or around the time of birth and can be caused by a variety of factors, as listed in Box 6.1. A congenital abnormality could be genetic or developmental, as long as it is present at or around the time of birth. Genetic and developmental conditions not obvious at birth can become manifest later in life. This chapter focuses on an overview of developmental and genetic concepts and a description of the more common developmental and genetic disorders. Specific dental disorders are discussed in those chapters that are associated with the clinical appearance of the conditions. Table 6.1 lists the most common developmental and genetic dental disorders and the chapters in which they are found.

BOX 6.1 Etiologies of Congenital Abnormalities

The etiology of most congenital abnormalities is unknown, with genetic conditions accounting for the largest number of known causes.

Causes of congenital abnormalities

Unknown	70%
Genetic	20%
Cytogenetic diseases (Chromosome abnormalities)	4%
Drugs, chemicals, radiation	2%
Maternal infection	2%
Maternal metabolic factors	1%
Birth trauma and uterine factors	1%

From Rubin R, Strayer DS, Rubin E, eds. Rubin's pathology: clinicopathologic foundations of medicine. 6th ed. Baltimore: Lippincott Williams & Wilkins, 2012. Figure 6-1, p. 215.

Concepts of Developmental Abnormalities

Teratology is the study of developmental anomalies that take place during fetal development (Rubin et al., 2012). The agents that cause developmental anomalies are called **teratogens.** Teratogens can be chemical, biologic, or physical in nature. Table 6.2 lists some of the known teratogenic agents and examples of disturbances they may cause. Many of these abnormalities are due to errors in **morphogenesis,** which is defined as the time during which embryonic cells specialize or differentiate to become the organs and parts of the body. The human body is especially vulnerable to teratogenic agents during morphogenesis. Figure 6.1 indicates critical stages in the development of specific organs and systems. Development of the **fetus** technically starts at the end of the 8th week of gestation; prior to that the fetus is called an **embryo**. Errors in morphogenesis occurring in utero can take many forms, such as:

- Agenesis: The complete or partial absence of an organ or part of the body (i.e., missing third molars)
- Dysraphic abnormality: Anomaly caused by the failure of opposing structures to fuse (i.e., cleft lip and palate)
- Involution failure: The existence of embryologic structures (i.e., thyroglossal duct) that should have been eliminated by the body at a certain stage of development

TABLE 6.1 **Developmental and Inherited Oral Disorders**

Disorder	Type of Disorder	Chapter
Cyclic neutropenia	Genetic	Chapter 9
Peutz-Jeghers syndrome	Genetic	Chapter 10
Cherubism	Genetic	Chapter 10
Epidermolysis bullosa	Genetic	Chapter 11
Congenital hemangioma	Developmental	Chapter 13
Vascular malformations	Developmental	Chapter 13
Genetic hemorrhagic telangiectasia	Genetic	Chapter 13
White sponge nevus	Genetic	Chapter 14
Neurofibromatosis	Genetic	Chapter 17
Multiple endocrine neoplasia syndrome	Genetic	Chapter 17
Lymphangioma	Developmental	Chapter 17
Cervical lymphoepithelial cyst	Developmental	Chapter 17
Thyroglossal tract cyst	Developmental	Chapter 17
Dermoid cyst	Developmental	Chapter 17
Osteopetrosis	Genetic	Chapter 18
Gardner syndrome	Genetic	Chapter 19
Nevoid basal cell carcinoma syndrome	Genetic	Chapter 20
Hypophosphatasia	Genetic	Chapter 21
Osteogenesis imperfecta	Genetic	Chapter 21
Dentinogenesis imperfecta	Genetic	Chapter 21
Amelogenesis imperfecta	Genetic	Chapter 21

- Division failure: The failure of certain structures to divide or cleave during fetal development
- Atresia: Failure of a lumen to form, causing a structure that should be hollow to be constricted or solid, as in esophageal atresia, where the esophagus is fully or partially obstructed at birth
- Ectopia: The development of structures away from the normal site (Fordyce granules are ectopic sebaceous glands found in the oral mucosa)
- Dystopia: The failure of an embryologic structure to move into its final adult position during development (i.e., lingual thyroid)

TABLE 6.2 **Teratogenic Agents**

Listed are examples of teratogenic agents and some of the developmental/congenital abnormalities with which they are associated.

Teratogen	Example
Alcohol	FASD
Tobacco	Low birth weight, preterm birth, spontaneous abortion, sudden infant death syndrome
Cocaine	Preterm birth, growth retardation, central nervous system infarctions, seizures, genitourinary and gastrointestinal tract abnormalities
Heroin	Low birth weight, addiction at birth, learning disabilities, personality dysfunctions
Warfarin	Congenital central nervous system defects and nasal hypoplasia
Thalidomide	Absent or flipper-like arms and legs
Accutane (isotretinoin)	Craniofacial abnormalities, cleft lip and/or palate, micrognathia, cardiac and central nervous system abnormalities
Anticancer drugs	Multiple congenital abnormalities, spontaneous abortion
Tetracycline	Inhibited bone growth, intrinsic dental staining
Paramyxovirus (mumps)	Orchitis, oophoritis, male and female sterility
Maternal diabetes	High birth weight, neural tube defects, cleft lip and/or palate, respiratory distress syndrome, congenital heart defects
Maternal folic acid deficiency	Neural tube defects, anemia, cleft lip and/or palate
Systemic lupus erythematosus	Congenital heart block, stillbirth

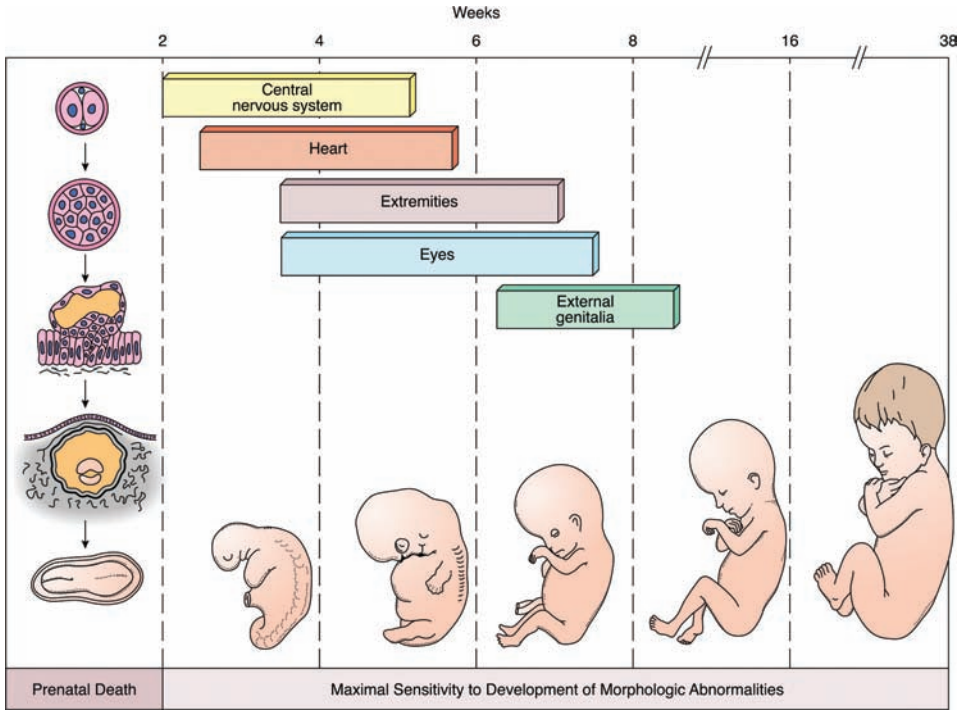


FIGURE 6.1. Sensitivity of specific organs to teratogenic agents at critical stages of human development. Exposure to teratogenic agents in the preimplantation and early postimplantation stages of development (**far left**) leads to prenatal death. Periods of maximal sensitivity to teratogens (**horizontal bars**) vary for different organ systems but overall are limited to the first 8 weeks of pregnancy. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

Teratogens can cause multiple abnormalities in multiple organs or systems, depending on whether exposure to them occurs when more than one developmental process is going on. Defects in multiple systems and/or organs can also occur when a single change takes place that affects other developmental processes farther along in time. Agenesis of the thyroid gland not only affects *embryogenesis* (development of the embryo) and fetal development but also causes *congenital hypothyroidism,* a developmental defect that severely stunts growth and causes mental retardation in the child (see Chapter 7). The effect of teratogenic agents is greatly reduced after the 12th week of gestation, when most of the crucial morphogenesis is completed.

Developmental Abnormalities

The following two examples of developmental abnormalities may be encountered during dental hygiene practice. Remember these are not representative of most errors in morphogenesis, which can be as harmless as a folded ear or as severe as anencephaly, in which the cranial vault is missing and the brain does not develop.

NAME: Fetal alcohol spectrum defects (FASD)

Etiology: FASD is an umbrella term describing the range of effects that can occur in a person exposed to alcohol, a teratogenic agent, during pregnancy (NOFAS, 2006). This is not a diagnostic term; it encompasses the following diagnoses:

- Fetal alcohol syndrome (FAS)
- Alcohol-related neurodevelopmental disorder (ARND)
- Partial fetal alcohol syndrome (PFAS)
- Alcohol-related birth defects (ARBD)

There is no specific amount of alcohol known to produce FASD nor is there a safe time to indulge in alcohol ingestion during pregnancy. Each individual is affected by alcohol differently; FASD may affect the child of a mother who drank only three beers a day on the weekends, while another child born to a woman who drank two beers a day throughout her pregnancy is not affected at all.

Method of Transmission: FASD cannot be transmitted from person to person.

Epidemiology: Not all diagnoses under FASD have statistical data available. FAS is estimated to occur in 1 to 2 infants in 1,000 live births. If this number included the number of children without the syndrome but with ARND, a milder expression of FAS with fewer abnormalities, the rate would climb to about 10 in 1,000 births (Vaux & Chambers, 2010; Olson et al., 2009). The incidence increases in children born to mothers who drink heavily during pregnancy. FAS affects all races but has a significantly higher incidence among Native Americans (Sarche et al., 2011).

Pathogenesis: Alcohol crosses the placenta and is maintained at the maternal concentration level for extended lengths of time. The alcohol is also stored in the amniotic fluid, increasing exposure of the fetus to the alcohol. The exact mechanism responsible for all of the abnormalities associated with this syndrome is not known (Vaux & Chambers, 2010).

Extraoral Characteristics: Three general groups of abnormalities must be present for a child to be diagnosed with FAS. The child must have growth deficits, at least three of the characteristic facial features, and neurodevelopmental problems. The list of potential abnormalities is extensive; only the most common and characteristic defects are discussed in this text. Children with FAS have microcephaly (a small head), are underweight at birth, short in length, and continue to be significantly shorter in stature than their peers throughout life. The characteristic facial features include narrow eyes (small palpebral fissures) with epicanthal folds, short nose with a turned-up end, and thin upper lip with an indistinct flat philtrum area (Fig. 6.2). Neurodevelopmental problems include the following: mild-to-moderate mental deficiency (lower IQ), attention deficit and hyperactivity disorders, learning disabilities, language impairment, poor coordination, poor judgment, behavior problems, and poor social skills. Other common problems include seizure disorders, eye disorders, hearing loss, congenital heart defects, and an increased risk for certain cancers (Vaux & Chambers, 2010).

Perioral and Intraoral Characteristics: In addition to the characteristic facial features discussed above, cleft lip and/or palate may be present.

FIGURE 6.2. Fetal alcohol syndrome. Child with FAS illustrating many of the characteristic facial features including short palpebral fissures, a wide and flattened philtrum, and thin lips. These children may also have cardiovascular and limb defects. (From Bickley LS and Szilagyi P. Bates' guide to physical examination and history taking. 8th ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

Distinguishing Characteristics: The facial features at birth are distinctive for this syndrome. As the child ages and progresses into adulthood these features become less obvious.

Significant Microscopic Features: Not applicable

Dental Implications: Knowledge of the facial features characteristic of FASD is very important. A dental professional may be able to connect the features with observable behavior and facilitate the diagnosis of a previously undiagnosed case. It is crucial to identify these individuals as early as possible to initiate intervention therapies to help them reach their highest potential. In addition, the dental hygienist has an excellent opportunity to counsel pregnant patients about the effects of alcohol on the unborn child. The dental professional should review the medical/dental history of a patient with FASD for any sign of congenital heart defects and determine what medications are being taken prior to initiating any dental treatment (Box 6.2).

Differential Diagnosis: Not applicable

BOX 6.2

Heart Defects and Dental Care

Infective endocarditis is a serious illness with numerous long-term health consequences including death. The source of this infection is usually bacteria that have found their way into the bloodstream, causing a bacteremia (bacteria in the blood). The oral cavity is a major source of bacteria. The oral environment is normally separated from the blood stream by mucous membranes. When these membranes become compromised or injured because of infection or trauma, bacteria are allowed to pass into the blood, creating a bacteremia. In a normal heart, this is usually not a problem; however, in the presence of heart defects that change the pattern of blood flow, bacteria may be allowed to colonize the endothelial surface of the heart in areas affected by the defect, resulting in endocarditis. Since 1955, the American Heart Association (AHA) has recommended a prophylactic antibiotic regimen prior to most dental procedures (those with a risk of compromising the mucosal barrier) for individuals who had heart defects they felt placed the person at a high risk of endocarditis, and for years, dentists and dental hygienists have monitored patient compliance with the prophylactic regimen and reappointed patients who failed to take their medication prior to their appointments. The type of heart defects covered and the recommended regimens have been modified several times since 1955. Until recently, the AHA recommended coverage for many types of heart defects; however, in 2007, it was determined that infective endocarditis was more likely to result from random bacteremias caused by daily activities such as eating, flossing, and brushing than from bacteremias caused by dental procedures. They concluded that, for most individuals, maintaining optimal oral health is more important in decreasing the risk of infective endocarditis than providing prophylactic antibiotics prior to a dental appointment (Nishimura et al., 2008). The dental hygienist is in a key position to educate patients about their risks and how to decrease them. More information on the specific heart defects and conditions for which prophylactic antibiotic premedication is still recommended and for a listing of the medications and dosages, please refer to Chapter 8.

Treatment and Prognosis: The damage done by alcohol exposure is permanent. Congenital defects such as heart defects and oral clefting can be corrected surgically. Behavior modification therapies and a structured learning environment that is sensitive to the needs of these children are crucial. Children are often treated with medications (Ritalin and others) used to alleviate behavioral symptoms that are similar to those seen in attention deficit disorder. Working with children who have FASD can be very difficult, but also very rewarding. The prognosis for these children is not measured in terms of life span but in terms of quality of life. Between the ages of 21 and 51, 95% have mental health problems, 55% are incarcerated or institutionalized for substance abuse or mental disorders, 60% are in conflict with the law, 82% cannot live independently, 70% have problems with employment, and 50% of men and 70% of women are struggling with their own alcohol or drug abuse problems (Streissguth et al., 2004; Vaux & Chambers, 2010).

NAME: TORCH syndrome

TORCH is an acronym referring to a number of pathogenic agents that cause similar developmental abnormalities in the embryo or fetus if the mother is infected with them during pregnancy.

Etiology: The organisms that cause the following infections are the etiologic agents for the disorders in this syndrome:

T—Toxoplasmosis
O—Other infections such as syphilis, tuberculosis, and varicella–zoster virus
R—Rubella
C—Cytomegalovirus
H—Herpesvirus

Method of Transmission: With the exception of herpesvirus, these infectious agents are transmitted to the fetus or neonate across the placenta or during passage through the birth canal. Herpesvirus does not typically cross the placenta and is almost always acquired during birth.

Epidemiology: In general, TORCH organism infections occur in about 1 to 5% of live births and are a major cause of abnormalities and death in neonates (Rubin et al., 2012).

Pathogenesis: Rubella, cytomegalovirus, herpes simplex virus, and varicella–zoster are all viral infections. Syphilis and tuberculosis are bacterial infections, and toxoplasmosis is caused by a protozoan. The mechanisms responsible for producing the pathology associated with the TORCH syndrome are not clear but result in similar manifestations.

- Toxoplasmosis: Transmitted most often vertically through the placenta to the developing fetus. Primary maternal infection occurring early in the pregnancy carries a higher risk of transmission than infections transmitted later in the pregnancy. About 30% of infants exposed to the organism acquire the infection; most are asymptomatic at birth but may show symptoms later in life or not at all (Brook et al., 2011).
- Other: Syphilis—Transmitted vertically from mother to fetus across the placenta. Approximately 90% of infants of untreated mothers with primary or secondary untreated syphilis will develop the infection. More information on the pathogenesis of syphilis can be found in Chapter 12. Tuberculosis—Transmission of tuberculosis occurs through the blood across the placenta or when the fetus aspirates infected amniotic fluid. Symptoms develop within the first 2 or 3 weeks of life. Varicella–zoster—Transmission occurs when a maternal viremia carries the virus across the placenta, infecting the fetus. Approximately 2% of exposed fetuses will develop congenital varicella syndrome. More infections such as listeriosis, group B streptococcus, and leptospirosis are included in the list but are very rare.
- Rubella: Maternal infection with rubella may cause a viremia that can transport the virus across the placental barrier causing congenital rubella syndrome. The earlier the infection occurs during pregnancy, the more serious the manifestations.
- Cytomegalovirus (CMV): CMV is transmitted across the placenta or through aspiration of vaginal secretions during birth. Ten percent of those exposed will have clinical evidence of the infection at birth. The most severe manifestations are called cytomegalic inclusion disease (Schleiss, 2010).
- Human herpes simplex virus (HSV): HSV-2 is transmitted most often during birth through exposure to vaginal secretions in the birth canal although it may cross the placenta in rare cases. Infants of mothers who have a primary infection during pregnancy are at highest risk of acquiring the infection (Corey & Wald, 2009).

Extraoral Characteristics: General characteristics associated with defects caused by most of the TORCH agents include the following: premature birth, encephalitis, microcephaly, hydrocephaly, mental deficiency (mental deficiency caused by congenital CVM infection is second only to Down syndrome [Schleiss, 2010]), hearing loss, visual impairment, enlarged liver, anemia, thrombocytopenia (bleeding disorder), rash, petechiae and bruising, congenital heart diseases, and pulmonary problems (Rubin et al., 2012). There are additional abnormalities associated with each specific organism; however, only those occurring in the oral cavity are mentioned here.

Perioral and Intraoral Characteristics: Congenital syphilis will cause the permanent incisors to have a notched incisal edge, called *Hutchinson incisors*, and the first permanent molars to have an abnormal occlusal surface that looks like a cluster of berries, thus the name *mulberry molars* (Fig. 6.3). See more pictures of mulberry molars and Hutchinson incisors in Chapter 21. Perinatal herpes

FIGURE 6.3. Oral manifestations of congenital syphilis, one of the TORCH syndrome disorders. **A.** Hutchinson incisors. **B.** Mulberry molars. (From Sweet RL, Gibbs RS. Atlas of infectious diseases of the female genital tract. Philadelphia: Lippincott Williams & Wilkins, 2005.)

infections can present with vesicular lesions on the oral and perioral mucosa.

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: Dental considerations should focus on both necessary treatment modifications associated with elements of the syndrome and preventive education. The presence of congenital heart defects may increase the risk of infective endocarditis; thus education should focus on maintaining a healthy oral environment to decrease the risk of bacteremia (Box 6.2). In addition, pregnant patients should be counseled about preventing TORCH complex, including such information as the need for appropriate vaccinations, the need to be cautious around substances that could contain or harbor toxoplasmosis (unwashed fruits and vegetables, raw or undercooked meat), and the need to wash hands after gardening or handling cats or cat litter to remove the protozoan that causes toxoplasmosis (Furtado et al., 2011). Other concerns surround eating commercially prepared foods and deli foods like hotdogs that may not have been cooked correctly or might be contaminated because of inadequate sanitary conditions where they were prepared. Pregnant patients could be referred to the Centers for Disease Control (CDC) or other agency for more information.

Treatment and Prognosis: The best treatment for this syndrome is prevention. Hutchinson incisors can be crowned or otherwise esthetically restored to make them look normal; mulberry molars do not normally require any treatment. Prognosis also depends on the specific abnormality involved, such as mental deficiencies, sensory losses, and heart defects.

Overview of Genetic Concepts

The science and technology of genetics are progressing at a phenomenal pace. More and more information about genes and the human **genome,** the genetic composition of a haploid set of human chromosomes, is being discovered every day. In April 2003, the National Institutes of Health (NIH) and the U.S. Department of Energy (DOE) completed the Human Genome Project (HGP), which resulted in finding and mapping approximately 20,000 to 25,000 genes to their locations on specific chromosomes (HGP, 2005). Health care professionals are responsible for integrating this information into their specific professions. The National Coalition for Health Professional Education in Genetics (NCHPEG) released a newly revised set of Core Competencies in Genetics in 2007. The competencies encompass not only knowledge, but skills and attitudes related to genetics. A complete copy of this document may be obtained from the NCHPEG web site listed in the Media Menu at the end of this chapter. The curriculum in most dental hygiene programs does not allow complete coverage of this topic at this time; however, the Coalition suggests a minimum standard of knowledge as stated in Box 6.3. The information and activities in this text are focused toward helping students meet this standard.

Health professionals should be able to facilitate the genetic counseling process and prepare patients and families for what to expect, communicate relevant information to the genetics team, and follow up with the patient after genetic services have been provided. Genetic information may have far-reaching psychological and social implications and, unless fully trained, the health professional should not provide patients with any form of counseling related to genetics; instead, they should refer the patient to a certified genetic counselor.

BOX 6.3 **The Minimum Standard for Genetics Education**

The National Coalition for Health Professional Education in Genetics has proposed a minimum standard for current genetics education.

Each health care professional should at a minimum be able to:

- Examine one's competence of practice on a regular basis, identifying areas of strength and areas where professional development related to genetics and genomics would be beneficial
- Understand that health-related genetic information can have important social and psychological implications for individuals and families
- Know how and when to make a referral to a genetics professional

Taken from Core competencies in genetics for health professionals, National Coalition for Health Professional Education in Genetics (2007). Available at: *http://www.nchpeg.org/index.php?option=com_content&view=article&id=94&Itemid=84*

APPLICATION **6.1**

Genetics and Dentistry

Information from the Human Genome Project (HGP) has an impact on the practice of dentistry. The most obvious use for this information is in research to find ways to eliminate craniofacial, oral, and dental disorders and diseases with etiologies influenced by inherited traits. However, this is not the only use for this information. Dental professionals are aware of the intricate balance between bacterial pathogens in dental biofilm, the presence of predisposing/contributing factors, and the host response in the development of periodontal disease. Some of the predisposing/contributing factors include smoking, diabetes, nutrition, immune system dysfunction, and genetic predisposition. Much research has been and is being done to discover the exact genetic elements of periodontitis.

Specific gene mutations responsible for rare forms of syndromic periodontitis associated with Papillion-Lefèvre, Chédiak-Higashi, and Ehlers-Danlos syndromes have been identified and genetic tests have been developed to determine if these mutations exist in the individual. However, these forms of periodontitis are extremely rare; what is known about the most common form of periodontitis, chronic adult periodontitis, is much less clear.

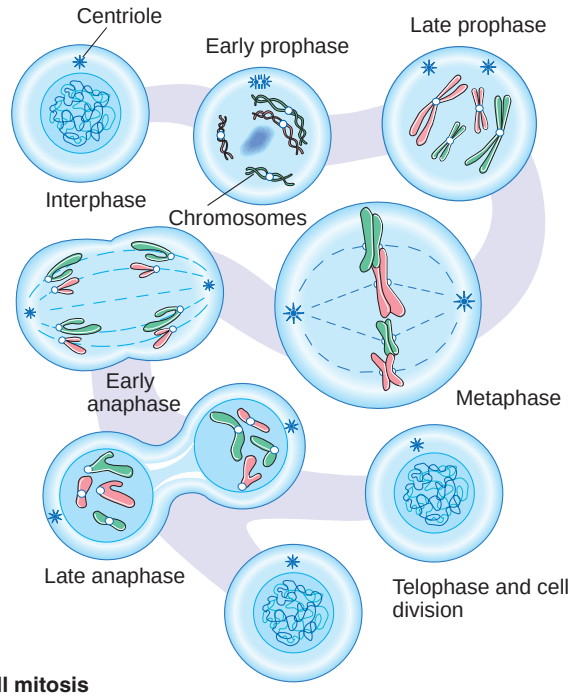
Research has indicated approximately 50% of susceptibility for chronic adult periodontitis may be due to genetic factors (AAP, 2005). The genetic influences are complex, involving the interaction of more than one gene and/or the additive effect of many genes and the environment. In addition, other elements such as time and behavioral factors ultimately play a significant role. Current models suggest the interaction of between 5 and 10 different genes, coupled with environmental factors such as smoking, nutritional status, and time, may be important in determining if an individual is susceptible to periodontal disease. It is a difficult task to determine which combinations of genes are likely to produce the conditions necessary to increase an individual's susceptibility for periodontitis. As research continues to be done it becomes clear that more research will be necessary to develop mechanisms or tests to identify individuals with an increased risk and prevent the disease before it develops. We must also remember that just because the individual's genetic makeup indicates they have an increased risk for periodontitis they may never develop it because environmental factors may not be conducive to producing disease. For example, an individual with immaculate oral hygiene and an excellent nutritional status may never develop periodontitis even if their genetic make-up places them at increased risk. The only genetic test commercially available for periodontitis risk is the Periodontal Susceptibility Test (PST). This test identifies the presence of a particular genotype involved with the overproduction of interleukins. Further research focusing on these genotype variations has not shown consistent results and the usefulness of the test has been questioned. The American Academy of Periodontology is not supporting the use of this test as a screening tool for periodontitis risk at this time (AAP, 2005).

Several studies have estimated 40 to 65% of an individual's risk for caries might be due to genetic factors (Ozturk, et al., 2010). One study looked at the *beta defensin 1* gene that is responsible for producing a group of antimicrobial peptides, beta defensins, involved with making epithelial surfaces resistant to bacterial colonization. They found one variation of the gene was related to an increased caries risk while another variation was associated with decreased caries risk (Ozturk et al., 2010). Another study found alpha defensins 1–4, produced by *alpha defensin 1–4* genes, associated with a decreased rate of caries in middle school children (Dale et al., 2006). The goal of research in this area is to develop a means to identify individuals with a high caries risk and intervene before damage is done.

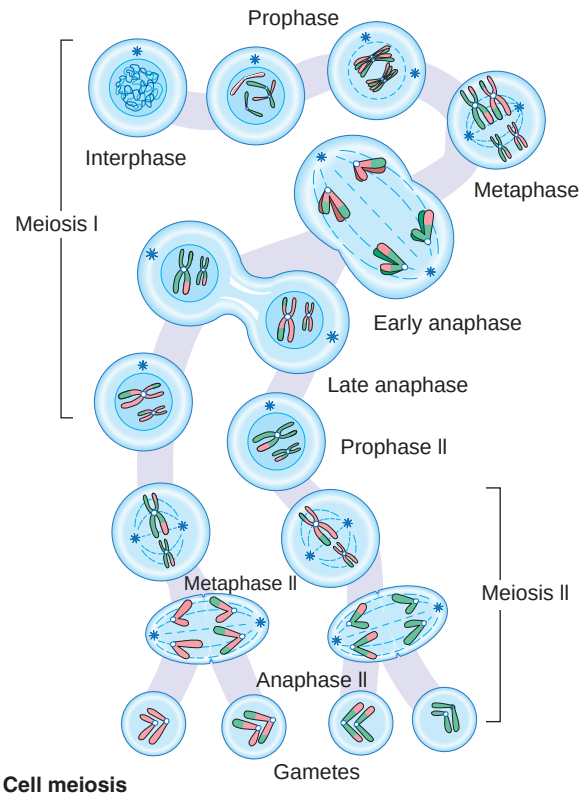
Another area of research focuses on the genetic makeup of the bacteria involved in dental diseases. In fact, an *effector* or mutated strain of *Streptococcus mutans* that does not produce the enamel-dissolving acid the original strain does has already been developed. The idea is to replace the original strain with the new effector strain that does not produce acid, thereby decreasing the potential for caries (Hein, 2005). It is the responsibility of the dental professional to keep informed about these developments and bring them into practice after their validity and usefulness have been determined.

Chromosomes

People inherit characteristics from their ancestors through genetic material contained within the sperm and egg cells contributed by each parent. The genetic material, **chromatin,** consists mainly of deoxyribonucleic acid (DNA) and is found in the nuclei of human cells. All human cells capable of dividing, other than sperm and egg cells, divide by mitosis, resulting in identical copies of the original cell. Sperm and egg cells divide by meiosis, resulting in genetically different cells containing only one-half of the genetic material needed for life. Genetic diversity of the human race is, in part, accomplished when half of the genetic material is supplied by the other parent at fertilization, resulting in the mixture of paternal and maternal genetic material. The phases of mitosis and meiosis are depicted in Figure 6.4. Chromatin is replicated during interphase. Just prior to cellular division, the chromatin wraps around a tightly configured group of proteins called a histone. Many of these form a tightly coiled structure called a **chromosome.** Each chromosome has a constricted area, or **centromere,** located at a point that is always constant for that chromosome. The centromere separates the chromosome into a short arm, or *p-arm,* and a long arm, or *q-arm.* During metaphase, the centromeres of two sister chromosomes (one original and one replicated) will join and attach the chromosomes to the spindle fibers. When joined together, each pair of sister chromosomes is called a single chromosome and each vertical half of that chromosome is called a **chromatid**



A. Cell mitosis



B. Cell meiosis

FIGURE 6.4. Stages of mitosis and meiosis. **A.** Mitosis results in the creation of an identical sister cell. **B.** Meiosis results in four haploid cells. In the female there is one egg and three polar bodies, and in the male there are four sperm cells created. (From Cohen BJ, Wood DL. Memmler's the human body in health and disease. 9th ed. Philadelphia: Lippincott Williams & Wilkins, 2000, with permission.)

(Fig. 6.5). The end of each arm of the chromosome or **telomere** (Fig. 6.6) appears to have a very important role in the reproductive capacity of most cells. Every time a cell undergoes mitosis, the telomeres get smaller; when they are almost gone, the chromosome's DNA becomes unstable, and the cell ceases to function. Scientists have discovered an enzyme called telomerase that is able to add more DNA to the telomere, effectively "resetting" the cell's clock. They are researching this concept, since it appears some cancer cells have the capacity to repair the telomeres, thereby preventing cell death and enabling uncontrolled reproduction. There is some evidence that stress may influence the length of the telomeres, shortening them prematurely and causing untimely apoptosis.

Human cells can be classified into two main types based on the number of chromosomes they contain: **somatic** cells and **gametes.** Somatic cells make up the human body from the top of the head to the tip of the toes. Each somatic cell has 46 chromosomes or 23 pairs of chromosomes, one paternal and one maternal set making these **diploid** cells. Gametes are the reproductive or sex cells, ovum and sperm. Each gamete has 23 single chromosomes, or half the genetic complement of a somatic cell, making the gametes **haploid** cells. To further define chromosomal makeup, each somatic cell contains 22 pairs of **autosomal** chromosomes that regulate almost everything the body is and does and one pair of sex chromosomes that not only determine sex but also have a few other important functions (see below). Each gamete has 22 single autosomal chromosomes and a single sex chromosome.

Sex Chromosomes

Sex chromosomes make up one pair of the 23 pairs of chromosomes. Males have one each of the X and Y (XY) chromosomes, while females have two X chromosomes (XX). The female carries two of each gene on the X chromosome. The male, however, carries only one X chromosome and thus has only one copy of the genes on that chromosome. Any **trait** (characteristic or attribute) controlled by a gene found on a man's X chromosome will be expressed because there is no second gene supplied by the father to stop its expression. Disorders such as Duchenne/Becker muscular dystrophy and color blindness are tied to genes located on the X chromosome and are seen most frequently in males because they inherit only the one defective gene (See Single-gene or Mendelian disorders, later in this chapter).

X Chromosome Inactivation

As noted above, females normally receive two X chromosomes, and males receive one. It could be presumed that women would therefore have a double dose of functioning genes on those chromosomes. However, this is not the case for most of the genes on the X chromosome. After

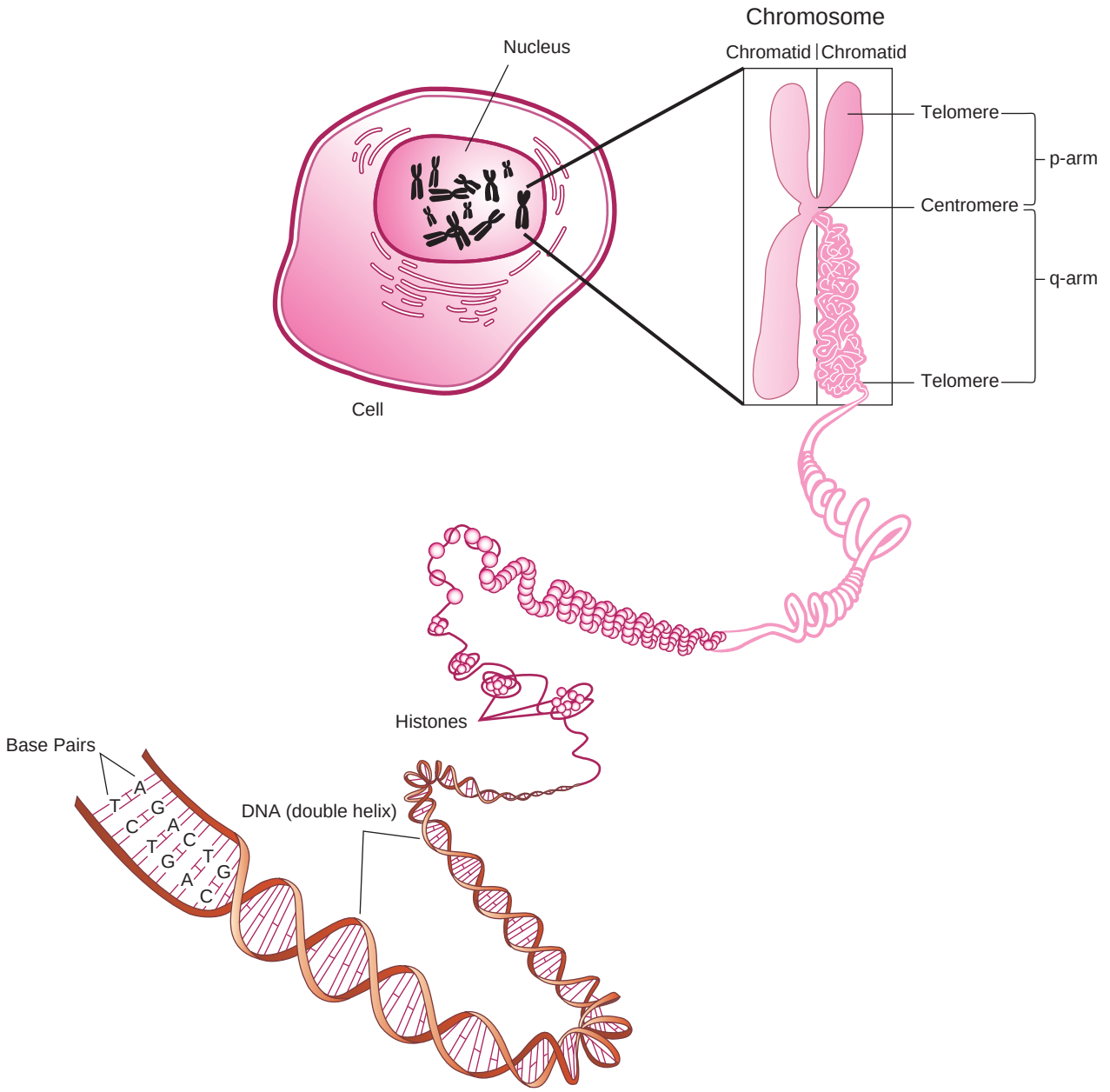


FIGURE 6.5. The chromosome during mitosis. Chromatin material coils into familiar chromosome structure prior to mitosis. The chromosome is composed of two identical chromatids joined at their constricted areas, or centromeres. The short arm created by the centromeres is the p-arm; the long arm is called the q-arm. The ends of each chromatid are called telomeres. (Courtesy of the National Human Genome Research Institute.)

researching this topic, in 1961 Mary Lyon proposed that approximately 7 to 14 days after fertilization one of the X chromosomes in each cell becomes inactivated, or turned off, and forms what is called a **Barr body.** This proposal is known as the *Lyon hypothesis* and has been proved correct. The Barr body (Fig. 6.7) is tightly compressed genetic material from the second X chromosome that is found close to the inner wall of the nuclear membrane and can be seen in cytology smears under a microscope but cannot be seen by the naked eye. Normal females have one Barr body per cell, normal males have none. There is no pattern as to which chromosome is inactivated in the cells of the embryo; one cell may inactivate the X chromosome contributed by the mother, while another will inactivate the X chromosome contributed by the father. The inactivation is permanent, and all cells developing from that embryologic cell will have the same inactive X chromosome, meaning an adult woman will have somatic cells containing either an active X chromosome from her mother or one from her father but not both (Rubin et al., 2012). To make matters even more interesting, not all of the genes on the inactive chromosome are inactive. Approximately 15 to 25% of genes on the inactivated X chromosome are active to some degree in all women (Carrel & Willard, 2005). Some of these genes

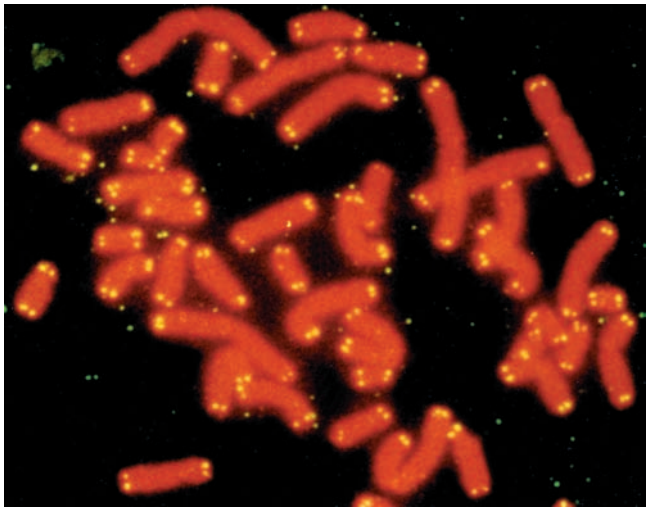


FIGURE 6.6. Telomeres. Chromosomes stained to show the telomeres. (Courtesy of Robert Moyzis, University of California, Irvine, CA; U.S. Department of Energy Human Genome Program.)

remain active in the Barr body allowing women to have the same total active gene count as men; however, many more remain active than necessary to "even the count." Researchers are studying the implications of this to determine if there is any medical significance especially as it relates to gender differences in illness and susceptibility to disease.

Genes

The genetic material in the chromosomes is arranged into areas that function as a unit to create a specific protein or enzyme. This functional unit is called a **gene.** The location of the gene on the chromosome is called the **locus.**

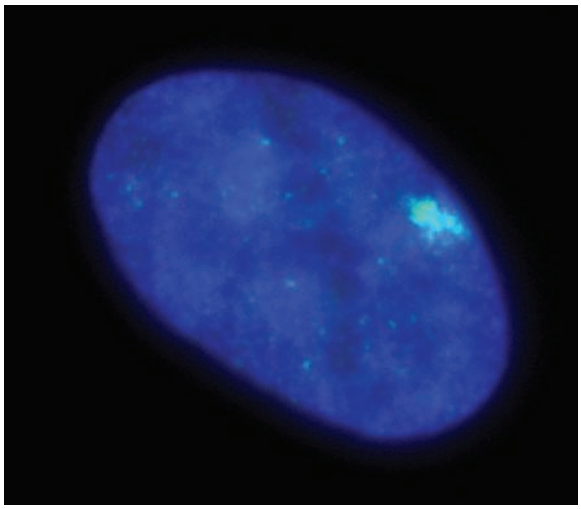


FIGURE 6.7. Barr body. Every normal female somatic cell contains one Barr body within the nucleus. This is a micrograph of a fibroblast nucleus. The dense spot at the nuclear periphery is the Barr body. The Barr body stains more intensely because the DNA of the inactive X is more compact. (Courtesy of Gayle Pageau.)

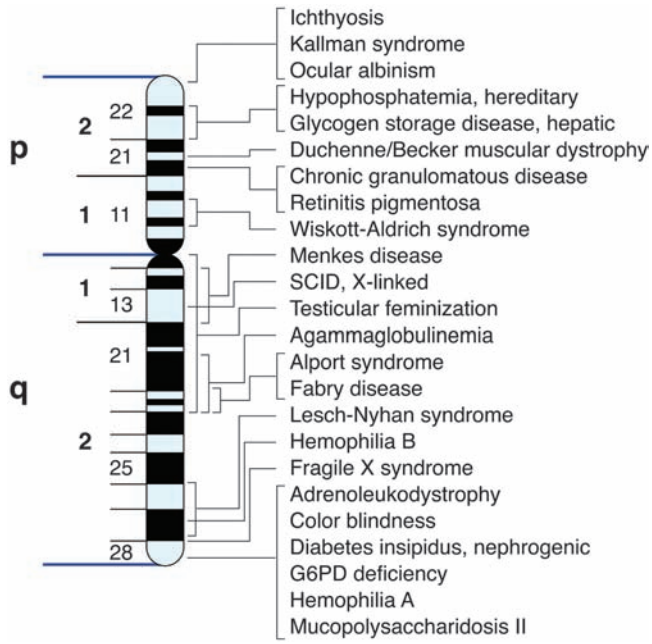


FIGURE 6.8. X chromosome with the loci of specific genes identified. The location of representative inherited disorders on the X chromosome. Genes that are located at the same locus on homologous chromatids are called alleles. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

Thus the maternal genes for eye color and the paternal genes for eye color would be located at the same locus on opposing chromatids of a chromosome. The gene involved with a specific single gene disorder would be found at the same locus of opposing chromatids as well (Fig. 6.8). Each opposing gene is called an **allele** of the other; together they are called alleles. The arrangement of alleles is crucial to another process that occurs during prophase I of meiosis when alleles are randomly exchanged from one chromatid to the sister chromatid in a process called chromosomal crossover. As chromosomes are paired up during prophase I, they will form contact areas between them called chiasmata (chiasma—singular). The chiasmata are the points at which chromosomal crossover (the exchange of genetic material between the two homologous chromosomes) will occur. The process is completed by the end of prophase I. Chromosomal crossover is one of the final phases of genetic recombination that helps to ensure genetic diversity within the human race. Figure 6.9 depicts the process of chromosomal crossover. A **karyotype** is a picture of a collection of the 46 chromosomes from one of an individual's cells. One of the purposes of a karyotype is to show whether an individual has too many or too few chromosomes (Fig. 6.10).

Elements of Genetics

The genetic makeup of an individual consisting of the genes on all 46 chromosomes is called the **genotype** of the individual. How the specific individual's body functions and what the person looks like physically is called

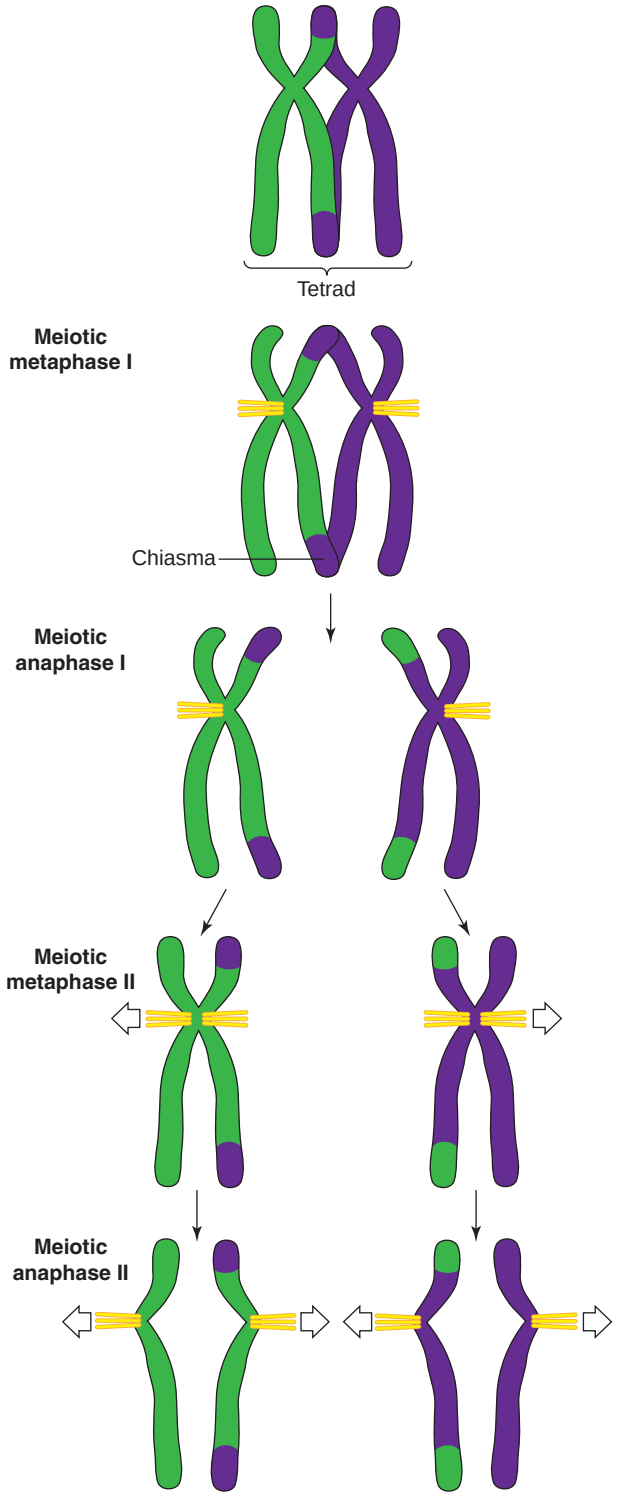


FIGURE 6.9. Crossing over of DNA at the time of meiosis. As chromosomes are paired up during first meiosis they will form contact areas between them called chiasmata (chiasma—singular). The chiasmata are the points at which chromosomal crossover will occur. During crossover, there is an exchange of genetic material between the two homologous chromosomes. The process begins early in prophase I of meiosis and is completed by the end of prophase I. Chromosomal crossover results in combinations of maternal and paternal DNA that are different from the parent cell being distributed in the egg and sperm cells formed in meiosis. This process is one of the final phases of genetic recombination that helps to ensure genetic diversity among the species.

the **phenotype.** When the alleles at a specific locus are identical, the individual is said to be **homozygous** for that genetic trait when they are different, the individual is **heterozygous** for the trait. Some genes are **dominant,** that is, they will express the trait whether the individual is homozygous or heterozygous for that trait. To the contrary, identical **recessive** genes must be present in both alleles for a recessive trait to be expressed. An individual who is heterozygous for a particular genetic trait may be a **carrier** of a recessive trait, disorder, or disease. Carriers do not usually exhibit characteristics of the gene in their phenotype, but they are able to transmit the gene to the next generation. If the partner of the carrier is also a carrier, then it is possible to have a child who will exhibit the full phenotypic expression of the recessive trait. Occasionally carriers will benefit from being heterozygous or having one recessive gene and one dominant gene, as is the case with sickle cell trait (see Chapter 9), where the affected individual is protected from contracting malaria.

Intermediate expression occurs when an individual who is heterozygous for a particular trait exhibits neither of the homozygous phenotypes but exhibits a trait somewhere between the two. For example, male voice pitch is controlled by a specific gene; when the alleles are homozygous, the voice is either a high or low pitch, when the alleles are heterozygous the voice is a baritone or middle range. Both alleles of the same gene can be equally expressed through **codominance.** An example of codominance can be seen in the inheritance of blood type. An individual who has the allele for type A and the allele for type B blood will exhibit type AB blood. Two other concepts important for understanding how an individual exhibits genetically controlled traits are penetrance and expressivity. **Penetrance** refers to the number of people who have the genotype for a specific trait and who exhibit the expected characteristics or phenotype. *Complete penetrance* describes a genotype that is always portrayed in the phenotype. *Incomplete penetrance* refers to the number of individuals who have the same genotype as above but who do not exhibit the characteristics or the phenotype expected. They may transmit the genetic trait to the next generation, who also may or may not exhibit the expected phenotype. **Expressivity** refers to variations with which individuals even within the same family may exhibit the phenotype of an identical genetic trait. Refer to Table 6.3 for an example of how these traits are expressed in the phenotype of individuals.

Genetic Disorders

There are two potential sources of genetic disorders: the chromosomes and the genes contained within them. Chromosomal abnormalities can involve either the *number* of chromosomes or the *structure* of the chromosome. Disorders caused by gene abnormalities can be inherited from one or both parents, or they can be the result of a spontaneous mutation in a gamete or an early fetal cell.

Every time a cell divides there is potential for something to go wrong. As discussed above, a small number of human

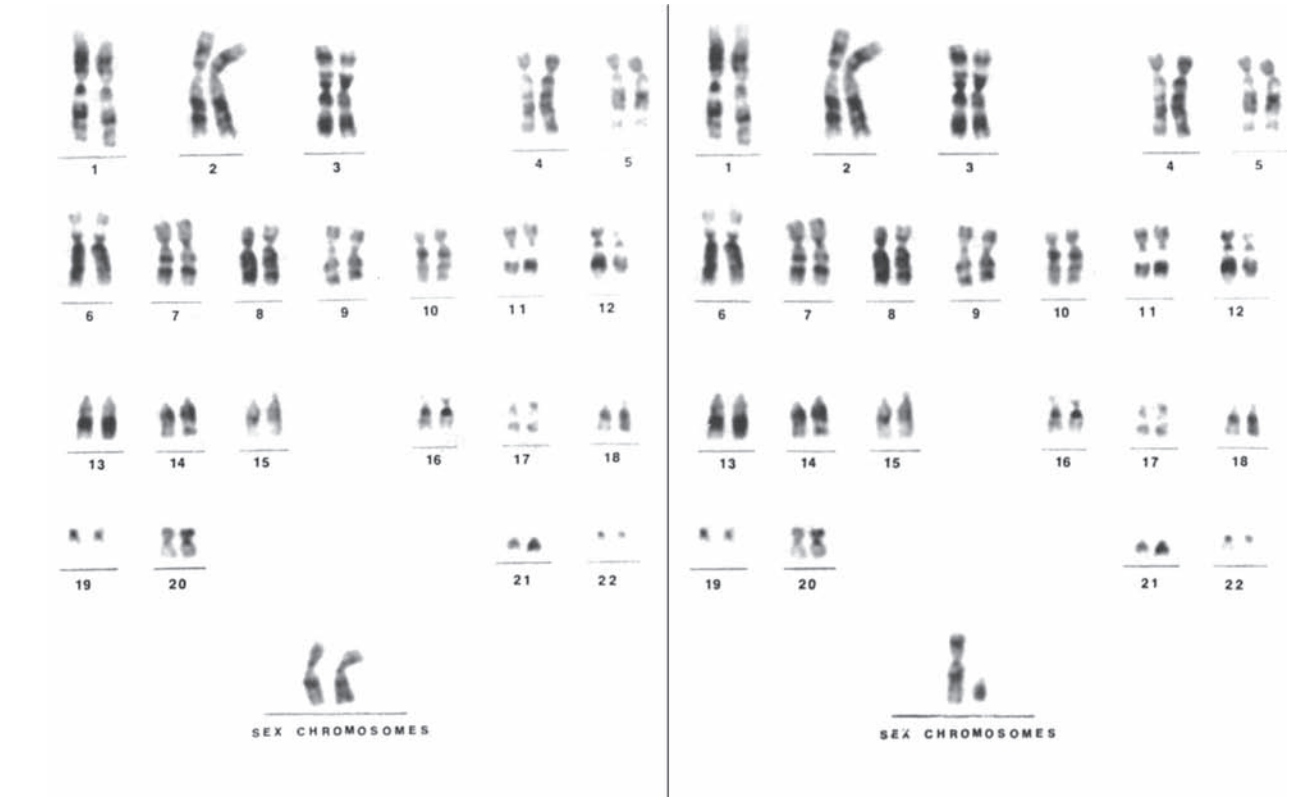


FIGURE 6.10. Normal male and female karyotypes. Photomicrographs of human chromosomes arranged in a standard classification. If a blood sample is taken from a child or adult and the white blood cells are examined at the mitotic division phase of reproduction, transferred to slides, and photographed under high-power magnification, the individual chromosomes can be cut from the photograph and arranged according to size and shape. **A.** Normal female karyotype. **B.** Normal male karyotype. (From Pillitteri A. Maternal and child nursing. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

APPLICATION 6.2

Did you know…?

- An entire copy of the human genome, or three billion base pairs, is contained in each and every human cell with a nucleus.
- In most cases, if there is a defect that cannot be repaired in the DNA of a cell, it will be scheduled for programmed death or apoptosis.
- A system called epigenetics determines when some genes are turned "off" or "on" before they are passed to the next generation. This influences the traits the individual will express in his or her phenotype. The status is permanent for the person the genes are passed to but when the same genes are passed to a second generation the turned "off" genes might be turned "on" and visa versa.
- Polymorphisms are slight genetic changes that occur in more than 1% of the population. Common enough to be considered a normal variation in the DNA, polymorphisms are responsible for many normal differences between individuals such as eye color, hair color, and blood type. Although many polymorphisms have no negative effect on a person's health, some of these variations may influence the risk of developing certain disorders such as caries and periodontal disease (see Application 6.1).
- Thirty-seven human genes are located in the mitochondria of each human cell. Mitochodrial DNA is inherited exclusively from the mother, allowing researchers to trace maternal lineage far back in time. Some say it may be possible to trace mitochondrial DNA back to the origin of humanity.
- Gene therapy often uses a viral vector to insert a specific DNA change into the cells of the person undergoing treatment. The vector is modified so as not to cause disease but at this time ethical concerns make this therapy available only when there is no other treatment for the disease.
- Genetic discrimination occurs when individuals are treated differently by employers or insurance companies because they have a gene mutation that may cause an inherited disorder or place them at a higher risk for one. This may be one disadvantage of genetic testing.

TABLE 6.3 **Comparison of Genotype with Phenotypic Expression**

B, Blue hair (dominant) y, yellow hair (recessive)	**Genotype**	**Phenotype**	
Homozygous dominant	BB	Blue hair	
Heterozygous dominant	By	Blue hair	
Homozygous recessive	yy	Yellow hair	
Intermediate expression (blending)	By	Green hair	
Codominance (both B and y are expressed)	By	Blue and yellow hair	
Incomplete penetrance	By	Yellow hair	
Variable expressivity	BB or By	Navy blue hair	
		Periwinkle hair	
		Sky blue hair	

cells undergo genetic changes regularly. These cells are usually destroyed by the body or not allowed to replicate; thus there is little chance of catastrophic consequences. However, if that genetic change or mutation occurs in a gamete or in one of the very early cells in the **zygote** or **embryo,** the results can be disastrous, since all of the cells that are generated by the mutated cell will have the same mutation.

Abnormal Number of Chromosomes

A **euploid** cell has the correct number of chromosomes. As mentioned above, autosomal cells have 46 chromosomes (one pair each of 23 chromosomes) and are called diploid cells. Gametes have 23 single chromosomes and are called haploid cells. Both gametes and autosomal cells with the correct number of chromosomes are considered euploid cells. An autosomal cell with an entire extra set of chromosomes or 69 instead of 46 is a triploid cell; one with four sets or 92 is a tetraploid cell. Most pregnancies affected by either of these abnormalities will result in spontaneous abortion or stillbirth.

In some cases, cells may not have an entire extra set of chromosomes but may have one or more extra individual chromosomes, or they may be missing one or more individual chromosomes. This condition is called aneuploidy, and the abnormal cells are called **aneuploid** cells. **Trisomy** results when there are three of any chromosomes (Fig. 6.11), and **monosomy** results when there is only one chromosome instead of two. Monosomy of any of the somatic cells will not support life. Likewise, a zygote or cell resulting from conception that contains no X chromosomes will not survive. Generally, missing chromosomal material is much more serious than extra chromosomal material. Abnormalities in the number of chromosomes are usually caused by **nondisjunction,** or failure of paired chromosomes to separate and migrate to opposite poles during anaphase. This process creates monosomy in the cell without the chromosome and trisomy in the cell with too many chromosomes.

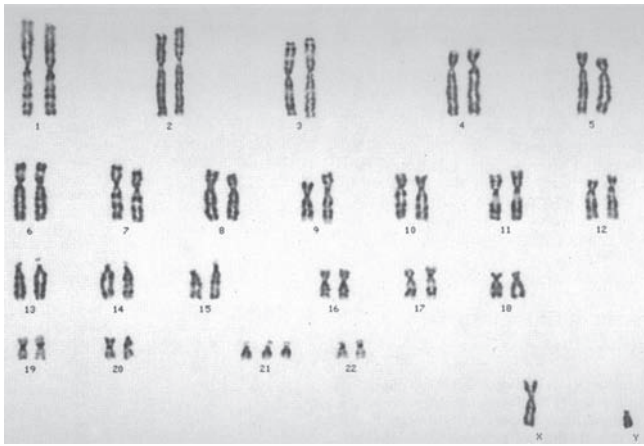


FIGURE 6.11. Karyotype of Trisomy 21. Trisomy 21 in the karyotype of a child with Down syndrome. All other chromosomes are normal. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

Abnormalities in Chromosome Structure

Not only can an abnormal number of chromosomes cause disorders, but also the structure of a chromosome can be altered in a way that will cause disorders. Structural abnormalities are caused by chromosome breakage, followed by a rearrangement or loss of the parts that broke off. The cause of these structural abnormalities is mostly unknown, but exposure to radiation, viruses, and other environmental agents is being studied. Several of the more common structural changes are listed below.

- **Deletion** occurs when a portion of a chromosome is lost. Deletion can occur any time there is a break in a chromosome (Fig. 6.12A).
- **Translocation** occurs when parts of two chromosomes are exchanged (Fig. 6.12B). For example, the short arm of chromosome 4 is exchanged with the long arm of chromosome 5.
- **Inversion** occurs when there are two breaks in a chromosome and the resulting piece is inverted or turned around and reinserted in the same place (Fig. 6.12C).

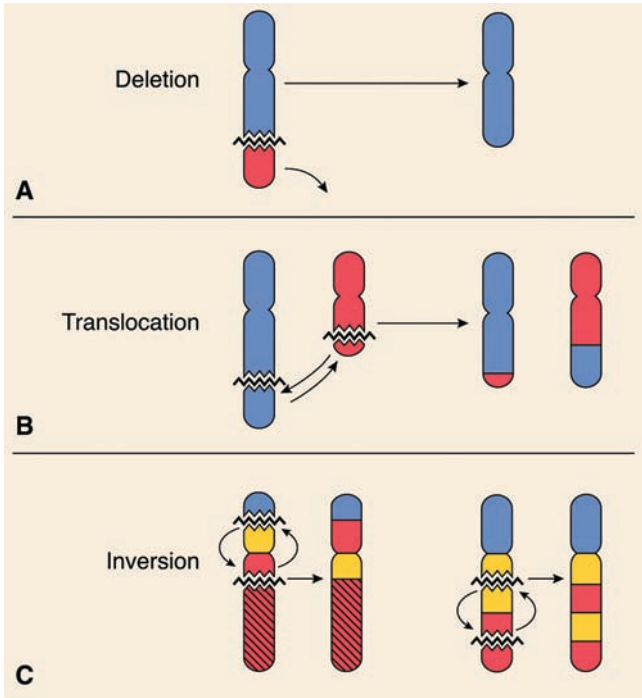


FIGURE 6.12. Abnormal chromosome structures. **A.** Deletion of genetic material results in a shorter chromosome with missing genetic material. **B.** Translocation occurs when there is a break in two chromosomes and the genetic material is switched between them. **C.** Inversions occur when there are two breaks in the same chromosome and the resulting piece of genetic material is turned upside down and reinserted. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

In translocation and inversion, there is no loss of genetic material, and the individual will function normally; however, when egg or sperm cells are produced, abnormal cells containing either too little genetic material or too much genetic material will result.

Mosaicism

When an egg is fertilized, the resulting diploid cell divides into two cells and then again into four cells and so on. Genetic **mosaicism** is created when a cell in the very early development of the embryo loses or gains genetic material. The amount of loss or gain can vary from an entire chromosome to a single gene. The cell losing or gaining the genetic material will continue to divide, but all of the future cells will have the identical genetic material. Thus an individual born with genetic mosaicism will have cells with two different karyotypes and a variable percentage of the abnormal cells mixed in with normal cells, depending on when the actual loss or gain of genetic material occurred in the development of the embryo (Fig. 6.13). Mosaicism is a key concept because it accounts for some of the variations that are seen in most genetic disorders. For example, classic trisomy 21, or Down syndrome, occurs when an individual is created from a fertilized egg that has an extra copy of chromosome 21. This individual will express the classic clinical signs of Down syndrome. If, however, the fertilized egg did not contain any extra genetic material but an error occurred in one cell after several divisions, then the individual who develops will have a mixture of normal and abnormal cells. This person would likely exhibit milder signs of Down syndrome than one who has all abnormal cells.

NAME: Trisomy 21 (Down syndrome)

Etiology: Chromosome disorder in which there is either one complete or one partial extra copy of chromosome 21.

Method of Transmission: Nondisjunction during the development of the egg accounts for about 95% of cases of trisomy 21. Translocation of the long arm of chromosome 21 to another chromosome accounts for 5%, and mosaicism accounts for 2% (Rubin et al., 2012).

Epidemiology: There are approximately 400,000 individuals with trisomy 21 living in the United States. Trisomy 21 will occur in one of approximately 691 live births. The incidence of trisomy 21 increases with the age of the mother; at 25 there is a 1:1,200 chance of trisomy 21, 1:350 at 35, 1:100 at 40, and 1:30 at 45 (NDSS, 2011). Eighty percent of children with Down syndrome are born to mothers under age 35 because more babies are born to this age group. Trisomy 21 affects males and females equally. Race and socioeconomic status of the parents is not considered to be a factor in the occurrence of this disorder. Once a child with trisomy 21 has been born, there is a 1:100 chance that a future pregnancy will result in another child with the syndrome (March of Dimes, Down syndrome, 2009).

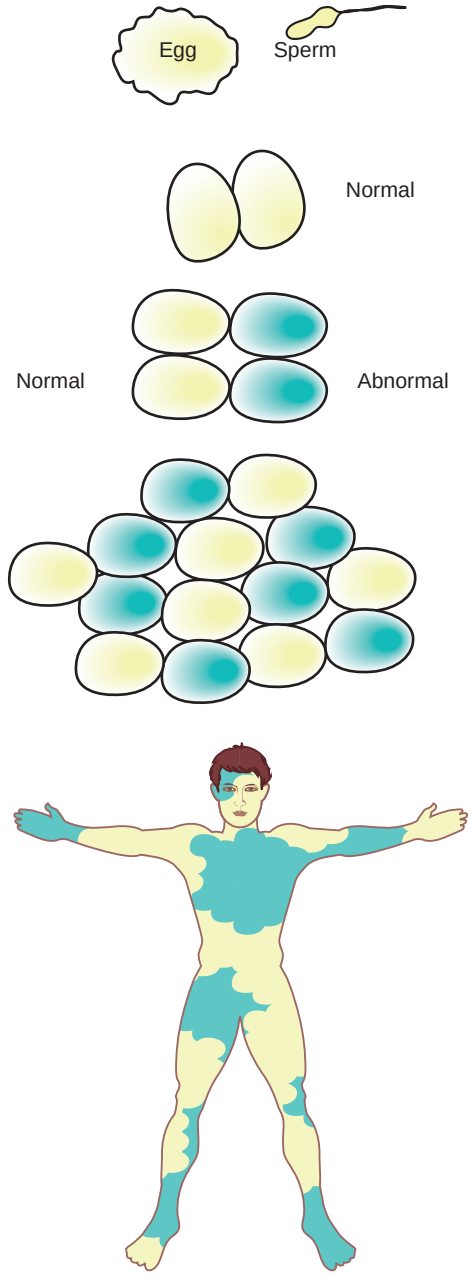


FIGURE 6.13. Mosaicism. Mosaicism is created when an error in early embryologic cell division causes the development of two different genotypes within the same individual. The earlier the error occurs, the higher the number or percentage of abnormal cells. Individuals who are mosaic for a particular genetic abnormality may not exhibit the full range of symptoms associated with the abnormality or may exhibit all of the symptoms but to a lesser degree.

Pathogenesis: The extra genetic material from the third chromosome may cause overproduction of important proteins associated with those genes. Chromosome 21 contains from 200 to 250 genes, and there are more than 9 genes on this chromosome that, if overexpressed, could lead to the development of the characteristic features seen in trisomy 21 (OMIM #190685, 2011).

Extraoral Characteristics: Individuals with trisomy 21 are affected with varying degrees of mild-to-severe mental

deficiency, which progresses as the individual ages. In addition, virtually all individuals will exhibit brain abnormalities consistent with those of Alzheimer disease and over half will manifest clinical signs of dementia as they grow into their 40s and 50s.

Congenital heart defects are seen in at least 33 to 50% of cases. Most of these involve defects between the chambers of the heart (Rubin et al., 2012). There appears to be an increased susceptibility to infections, but research has found no clear pattern of defects. Still, respiratory infections are unusually common and severe in this group; the most common are upper respiratory infections, ear infections, bronchitis, and pneumonia (March of Dimes, Down syndrome, 2009). Ninety percent of affected individuals have varying degrees of hearing and vision problems. Leukemia is seen 10 to 20 times more often in the trisomy 21 population than in the general population (OMIM #190685, 2011).

Individuals with Down syndrome are shorter than normal, with poor muscle tone and lax joints. Their hands are stubby, with a shorter than normal little finger and a single transverse crease across the palm called a **simian crease**. The face appears flat with a prominent forehead. The eyes are set close together (**hypotelorism**) and slant upward. There is a fold of skin beginning at the root of the nose and extending to the beginning of the eyebrow called an **epicanthal fold** (Fig. 6.14).

Perioral and Intraoral Characteristics: Hypoplasia, or underdevelopment of the midface, is characteristic of trisomy 21. The bridge of the nose is flattened. The frontal and maxillary sinuses may be smaller than normal or entirely absent. The palate is high, narrow, and shortened from anterior to posterior, contributing to the appearance of mandibular **prognathism,** or protrusion, because the mandible has developed normally. Individuals often have posterior crossbites and severe crowding of the anterior teeth. Patients with trisomy 21 have a characteristic open mouth posture considered to be the result of a small nasopharynx and enlarged tonsils and adenoids that compromise the upper air passages, resulting in mouth breathing. While there is no true **macroglossia** or enlarged tongue, the tongue does protrude because the mouth is so small. The tongue is usually fissured but has no definable central fissure.

Anterior open bites are very common and are thought to be caused by the lack of lip muscle tone and the pressure of the protruding tongue. Constant mouth breathing and the protruding tongue cause xerostomia and cracking and drying of the lips. Cleft lip and palate have a higher than average incidence.

Abnormalities of the dentition are common. Eruption of the primary and permanent dentition is delayed, and the eruption sequence may be abnormal (Regezi et al., 2008; Pilcher, 1998). Hypodontia, missing one or more teeth, in both primary and permanent dentitions is very common (Pilcher, 1998) as is abnormal tooth and root development and enamel hypocalcification. The caries rate in patients with trisomy 21 is approximately the same or slightly lower than in the general population (Pilcher, 1998).

The incidence of periodontal disease is reported to range from 60 to 100% in individuals with trisomy 21 under the age of 30 (Yoshihara et al., 2005). Possible immune system defects coupled with the presence of important periodontal pathogens is thought to be the underlying cause of the disease in this population.

Distinguishing Characteristics: The appearance of the face is the most distinguishing clinical feature of this syndrome.

Significant Microscopic Features: Not applicable

FIGURE 6.14. Trisomy 21. Typical features of a child with Down syndrome: (**A**) facial features; (**B**) horizontal palm crease (simian line).

Dental Implications: Dental professionals need to be careful in their initial assessment of the medical history of individuals affected by trisomy 21. If cardiac defects are present, the dental hygienist should educate the patient and caregivers about the risk of developing infective endocarditis from oral infections and the need to practice good oral hygiene to maintain healthy oral tissues. Preventive home care methods should be taught to the patient and caregivers, and frequent preventive care or maintenance appointments should be stressed to minimize the potential for a self-induced bacteremia. The severity of periodontal disease can be decreased and the process slowed with proper home care and regular periodontal debridement (Yoshihara et al., 2005). Care should also be used in preventing inhalation of oral pathogens to reduce the possibility of acquiring a respiratory infection.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Medical or surgical treatment for conditions such as heart defects is completed as soon as is practical. Cleft lip and palate are treated the same as for any child born with the condition. Children with trisomy 21 need to be followed closely by a team of health care providers including, but not limited to, those in the medical, dental, vision, hearing, and speech fields. Extensive cosmetic, orthodontic, and/or reconstructive treatments should be made available to the person according to what they can manage (Pilcher, 1998). The long-term periodontal prognosis is poor.

Life expectancy of a child born with this syndrome depends on the presence and severity of heart defects. Twenty-five percent of those with significant heart defects die before the age of 10, while only 5% without the defects die before age 10. After this age, the life expectancy is about 20 years less than in the general population, with only about 10% surviving into their 70s (Rubin et al., 2012).

NAME: Klinefelter syndrome (testicular dysgenesis)

Etiology: Classic Klinefelter syndrome is caused by an extra X chromosome in the male genotype (XXY). Variations of this grouping are possible and may include up to four extra X chromosomes.

Method of Transmission: The extra chromosomes seen in Klinefelter syndrome are due to nondisjunction in the egg cell in 50 to 60% of cases. The chances of this occurring increase as the age of the mother increases.

Epidemiology: Klinefelter syndrome occurs in about 1 of every 500 to 1,000 live births. It occurs equally across all races. However, by definition, it occurs only in males (Chen, 2011).

Pathogenesis: The abnormalities seen in Klinefelter syndrome are a result of altered male and female hormone levels. A deficit of testosterone results in underdevelopment or absence of secondary sexual characteristics at puberty. Levels of luteinizing and follicle-stimulating hormones are elevated because there is no production of testosterone and remain elevated because the negative feedback system keeps telling the hypothalamus that there is no testosterone and the hypothalamus keeps sending the signal to produce it. Each additional X chromosome increases the severity of the defects seen in this syndrome. An individual with a XXY genotype will have less severe manifestations than an individual with a XXXXY genotype.

Extraoral Characteristics: Individuals with Klinefelter syndrome are taller than usual, with long arms and legs (Fig. 6.15). Their intelligence is usually normal, but intellectual disabilities have been noted in individuals with more than one extra X chromosome. About half of affected individuals have mitral valve prolapse. The lack of proper sexual development in these individuals is the most obvious characteristic. No matter how many extra Xs are in the genotype, the phenotype will always be that of a male. However, the lack of testosterone results in little or no development of secondary sexual characteristics. Sparse facial and body hair, female pubic hair distribution, high-pitched voice, female fat distribution, small hard testes, and infertility are all characteristic of Klinefelter syndrome. Fifty percent or more have gynecomastia, enlarged breasts, and a 20 times higher chance

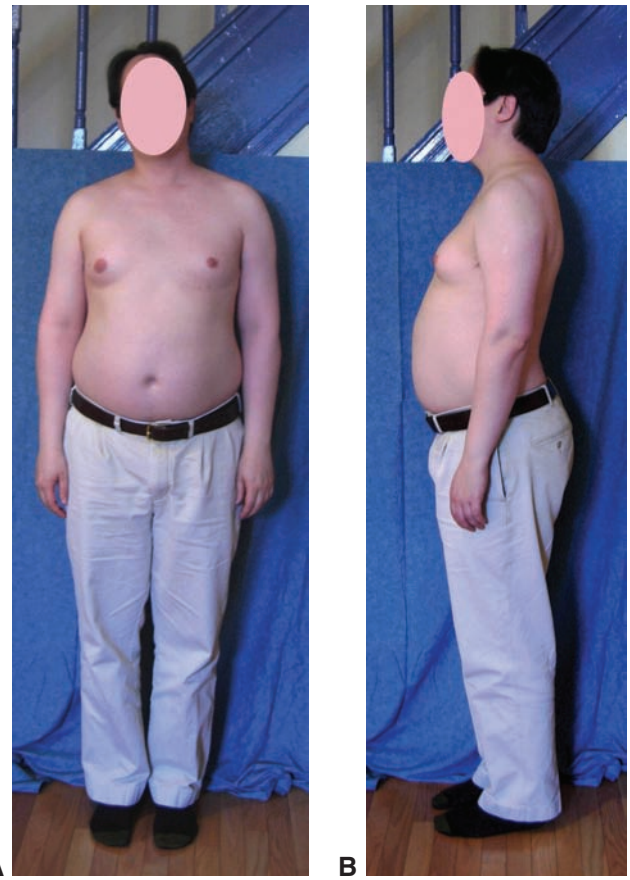


FIGURE 6.15. Klinefelter syndrome. Front (**A**) and side (**B**) views of a 38-year-old, 6-ft, 220-pound male with untreated Klinefelter syndrome (46,XY/47,XXY mosaic). Note the long arms and legs, female fat distribution, gynecomastia and lack of or sparse facial and body hair. (Malcolm Gin/CC-BY-SA-3.0 (*http://creativecommons.org/licenses/by-sa/3.0/*). Available at: *http://en.wikipedia.org/wiki/File:Bodymorphproj_mkg_modA001_20070325_pos03.jpg*, accessed December 22, 2011.)

of developing male breast cancer than normal (Chen, 2011). They also have an increased lifetime risk of osteopenia and osteoporosis due to low testosterone levels (see Chapter 10).

Perioral and Intraoral Characteristics: Aside from possible feminization of the facial features, the maxilla may be hypoplastic, and the molars may exhibit taurodontism, enlargement of the pulp chamber, and relative shortening of the root (see Chapter 21).

Distinguishing Characteristics: The most obvious feature of this syndrome is the lack of male sexual development.

Significant Microscopic Features: Male cells do not normally contain any Barr bodies. Individuals with this syndrome will express one Barr body for each extra X chromosome contained in their cells.

Dental Implications: The medical history must be closely examined because of the high probability of mitral valve prolapse. If present, the dental hygienist should educate the patient and caregivers about the risk of developing infective endocarditis from oral infections and the need to practice good oral hygiene to maintain healthy oral tissues. Taurodontism is of no clinical significance and requires no treatment.

Differential Diagnosis: Not applicable

Treatment and Prognosis: This disorder is usually not identified until the lack of sexual development causes concern. Treatment should begin in puberty and focuses on hormone replacement therapy. Testosterone injections promote the development of more masculine features and help to prevent osteoporosis. Mastectomy may be necessary to treat significant gynecomastia. There should be no need for modifications in dental care. The life span of these individuals is the same as the general population (Chen, 2011).

NAME: Turner syndrome (monosomy X)

Etiology: Turner syndrome is caused by monosomy of the X chromosome, resulting in 22 pairs of autosomal chromosomes and one single X chromosome in a female genotype. This is the only monosomy that is compatible with life.

Method of Transmission: Turner syndrome is usually associated with an error in the paternal genetic contribution. Some are true monosomies caused by nondisjunction, while many if not most are mosaics (45, X/46, XX) or are missing portions of the second X chromosome. Individuals with mosaicism will not exhibit the entire range of abnormalities associated with Turner syndrome.

Epidemiology: Turner syndrome occurs in about 1 of every 2,000 live births (Postellon & Daniel, 2011). All of those affected are women, and all ethnic groups are equally affected. Only about 1% of fetuses with this genetic defect are carried to full term (TSSUS, 2004).

Pathogenesis: Almost all of the abnormalities seen in Turner syndrome are attributable to the absence of estrogen. Although there are school programs screening girls for short stature (below the 5th percentile) and other symptoms of Turner syndrome, like Klinefelter syndrome, diagnosis of Turner syndrome often does not occur until a girl fails to begin puberty at the normal age.

Extraoral Characteristics: Turner syndrome produces short women (5 ft and under) who have webbing of the neck (Fig. 6.16A), a low posterior hairline, and a wide chest with

A

B

FIGURE 6.16. Turner syndrome. **A.** A 3-year-old with Turner syndrome. Note the webbed neck. (From Nettina SM. The Lippincott manual of nursing practice. 7th ed. Lippincott Williams & Wilkins, 2001). **B.** Adult with Turner syndrome exhibiting eye abnormalities, low set ears and the characteristic webbed neck. (Copyright: Chrousos GA, Ross JL, Chrousos G, et al. Ocular findings in Turner syndrome. A prospective study. Ophthalmology 1984;91:926–928).

widely spaced nipples. They usually have no ovaries but do have a uterus. Without adequate hormonal replacement therapy they develop no secondary sexual characteristics. Fifty percent or more will have osteoporosis, even with hormone replacement therapy. Scoliosis is also very common. Coarctation of the aorta (see Chapter 8), aortic valve defects, and hypertension are common. Endocrine disorders (see Chapter 7), specifically type II diabetes (30 to 40%) and hypothyroidism (35%) occur more often than in the general public. Epicanthal folds and other ocular abnormalities as well as vision and hearing defects are common (Fig. 6.16B). Most individuals who have Turner syndrome have average or above average intelligence, but many have learning disabilities and a characteristic impairment of spatial and mathematic reasoning skills (TSSUS, 2004).

Perioral and Intraoral Characteristics: These individuals may have an unusually high number of melanotic macules on their skin in any area. They may have a high narrow palate and small mandible resulting in crowding and malocclusion. The secondary teeth may erupt early and often have short roots, thin enamel, less dentin, and simple crown morphology. Orthodontic treatment is often necessary and care should be taken to monitor for root resorption because of the short roots (Bondy et al., 2007).

Distinguishing Characteristics: The short stature, webbed neck, and low hairline are clinically distinguishing characteristics.

Significant Microscopic Features: Not applicable

Dental Implications: The medical history should be thoroughly reviewed to rule out the presence of heart defects, hypertension, and metabolic disorders. If any are noted, proper modifications in dental hygiene care should be taken. Undiagnosed girls with the characteristic features of this syndrome should be referred to a physician for evaluation. Girls who do not receive hormone replacement therapy will have the potential for social, psychologic, and medical problems throughout life. Orthodontic treatment should be considered early and parents should be advised to take the child for an evaluation as soon as possible (Bondy et al., 2007).

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment for Turner syndrome focuses on the clinical features. Growth hormone given at the appropriate times can increase height and estrogens will cause development of secondary sexual characteristics. Medications can control hypertension, diabetes, and hypothyroidism. Surgery can correct cardiovascular problems when necessary. Adequate calcium, exercise, and estrogen therapy can help prevent osteoporosis. Turner syndrome decreases life expectancy by about 10 years depending on the existing medical conditions, if any (Postellon & Daniel, 2011).

Single-Gene or Mendelian Disorders

Single-gene abnormalities occur on the molecular level and are not microscopically detectable. The abnormalities usually involve a change in the nitrogen bases of the DNA, for example, a substitution of one base pair for another, or one or more base pairs might be added to the DNA. The exact mechanism is beyond the scope of this text; however, elements that can increase the chance a mutation will occur have been discussed in Chapter 2 and earlier in this chapter.

Single-gene disorders usually affect the structure or presence of a particular protein or enzyme component of the body. These disorders can be divided into four groups:

- Autosomal dominant—Autosomal dominant disorders refer to single-gene abnormalities that are expressed clinically whether the individual is heterozygous or homozygous for the trait (Fig. 6.17A).

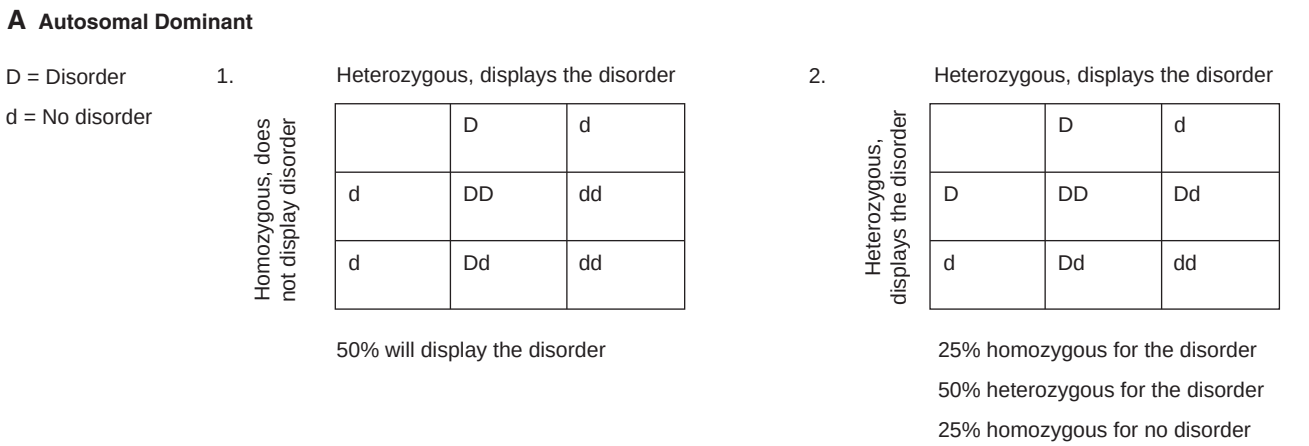


FIGURE 6.17. Inheritance patterns. **A.** Autosomal dominant inheritance. If an individual who is heterozygous for an autosomal dominant disorder mates with an individual who is homozygous for not having the disorder, you would expect 50% of their offspring to be heterozygous for the disorder and to exhibit it in their phenotype. If both partners are heterozygous for the disorder, then 75% of their offspring would exhibit the phenotype, with 50% having a heterozygous genotype and 50% having a homozygous genotype (25% for the disorder and 25% for not having the disorder).

B Autosomal Recessive

R = No disorder

r = Disorder

1.

Homozygous for the disorder, displays the disorder

Homozygous, for no disorder, does not display the disorder	r	r
R	Rr	Rr
R	Rr	Rr

All offspring are heterozygous for the disorder, not displayed

2.

Heterozygous for the disorder, does not display the disorder

Heterozygous for the disorder, does not display the disorder	R	r
R	RR	Rr
r	Rr	rr

25% homozygous for no disorder

50% heterozygous for the disorder, not displayed

25% homozygous for the disorder and display it

3.

Heterozygous for the disorder, does not display the disorder

Homozygous for the disorder, displays the disease	R	r
r	Rr	rr
r	Rr	rr

50% heterozygous for the disorder, not displayed

50% homozygous for the disorder and display it

C X-Linked Recessive

x = carries the disorder

X = does not carry the disorder

Y = does not carry the disorder

1.

Heterozygous female not displaying the disorder

Male with normal X	X	x
X	XX	Xx
Y	XY	xY

25% normal females

25% carrier females

25% normal males

25% males with the disorder

2.

Heterozygous female not displaying the disorder

Male with the disorder	X	x
x	Xx	xx
Y	XY	xY

25% carrier females

25% females with the disorder

25% normal males

25% males with the disorder

FIGURE 6.17. *(continued)* **B.** Autosomal recessive inheritance. If an individual who is homozygous for not having autosomal recessive disorder mates with an individual who is homozygous for the disorder, all of their offspring will have a heterozygous genotype and will have a normal phenotype. If the individuals are both heterozygous for the disorder, then 75% of the offspring will not exhibit the phenotype and 25% will exhibit the disorder. In the case of a homozygous and a heterozygous parent, 50% of the children would express the phenotype and 50% would not. The heterozygous offspring are carriers of the recessive disorder. **C.** X-linked recessive inheritance. A heterozygous female and a male whose X chromosome does not carry the disorder will produce male offspring who have a 50% chance of receiving the affected chromosome from their mother and exhibiting the disorder in their phenotype. The daughters have a 50% chance of becoming carriers of the disorder. An affected male and a heterozygous female would produce males who had a 50% chance of exhibiting the disorder just as above. However, now any female offspring has a 50% chance of being homozygous for the disorder and thus exhibiting the disorder.

- Autosomal recessive—Autosomal recessive disorders are associated with clinical symptoms only when both alleles at a given locus on **homologous**, or like, chromosomes are defective (homozygous). Both parents are usually heterozygous for the trait and appear clinically normal. Rare autosomal recessive disorders are often a product of consanguinity or inbreeding (Fig. 6.17B).
- Sex-linked dominant—A dominant sex-linked disorder will always be expressed whether the individual is heterozygous for the disorder or homozygous. In males, any gene found on the X or Y chromosome, aside from the 18 or so that are duplicated on both genes, will be expressed in the phenotype because there is only one copy.
- X-linked recessive—A recessive X-linked disorder will be expressed in the female only if she is homozygous for the trait, while the male will always express an X-linked recessive trait because he carries only one copy of the X chromosome (Fig. 6.17C).

Box 6.4 lists examples of common autosomal dominant, autosomal recessive, and major X-linked recessive disorders.

BOX 6.4

Common Examples of Autosomal Dominant Disorders, Autosomal Recessive Disorders, and X-Linked Recessive Disorders

Autosomal Dominant Disorders

Marfan syndrome
Ehlers-Danlos syndrome
Epidermolysis bullosa
Achondroplastic dwarfism
Hereditary hemorrhagic telangiectasia
Familial hypercholesterolemia
Von Willebrand disease
Retinoblastoma
Neurofibromatosis
Gardner syndrome
Multiple endocrine neoplasia syndromes I, II
Peutz-Jeghers syndrome
Familial dysplastic nevus syndrome
Huntington disease
Treacher Collins syndrome
Osteogenesis imperfecta (some types)

Autosomal Recessive Disorders

Cystic fibrosis
Tay-Sachs disease
Phenylketonuria
Albinism
Severe form of von Willebrand disease
Severe form of epidermolysis bullosa
Sickle cell anemia
A-thalassemia major

X-Linked Recessive Disorders

Hemophilia A and B
Duchenne muscular dystrophy
Red–green color blindness
Fragile X syndrome

Any trait linked to the Y chromosome and sex-linked dominant traits are very rare. This discussion focuses on the much more common X-linked recessive disorders important to dental/dental hygiene practice.

Refer to Box 6.5 for the major characteristics of inheritance patterns of autosomal dominant, autosomal recessive, and X-linked disorders.

Most of the traits observed in an individual's phenotype are not governed by one gene and therefore do not follow the four types of inheritance patterns just discussed. Two other types of inheritance, oligogenic and multifactorial, are also involved in the expression of an individual's inherited traits or phenotype. **Oligogenic inheritance** results from the interaction of more than one gene found at different loci either causing the phenotypic expression of a trait or modifying its expression by making it more or less severe. For example, many of the physical characteristics of humans such as eye color, hair color, tooth form, and skin color are the result of oligogenic inheritance (Beales et al., 2003). Multifactorial inheritance involves the interaction between genetic and environmental factors and is discussed later in this chapter.

Most of the following are common genetic disorders. Remember, individuals with these disorders may or may not express the full range of possible abnormalities.

BOX 6.5

Characteristics of Specific Inheritance Patterns

The major inheritance patterns associated with autosomal dominant, autosomal recessive, and X-linked recessive disorders are listed below.

Autosomal Dominant

- Males and females are equally affected
- The trait is expressed in the parents' phenotype whether they are homozygous or heterozygous
- There is a 50% chance that the offspring will be affected

Autosomal Recessive

- Males and females are equally affected
- Parents are usually heterozygous and phenotypically normal
- There is a 25% chance of the offspring exhibiting the trait, and a 50% chance that they will be heterozygous for the trait, or carriers

X-Linked Recessive

- Males with these disorders cannot transmit them to their sons
- Women who are carriers (Xx) have a 50% chance of transmitting the trait to their sons, who will be symptomatic
- Women who are carriers (Xx) have a 50% chance of transmission to their daughters, who will be asymptomatic
- All daughters of affected men are asymptomatic carriers, but the sons will be free of the abnormality and cannot transmit the disease to their children
- Symptomatic homozygous females result only from the rare mating of an affected male and an asymptomatic heterozygous or symptomatic homozygous female

NAME: Marfan syndrome

Etiology: Marfan syndrome is a connective tissue disorder caused by an abnormal gene (FNB1) on chromosome 15 that enables the production of a protein called fibrillin. Fibrillin is essential for providing strength and elasticity to certain connective tissues, especially those of the heart, blood vessels, eyes, and **periosteum** (connective tissue covering bones).

Method of Transmission: Marfan syndrome is transmitted in an autosomal dominant inheritance pattern in about 75% of cases. Spontaneous genetic mutations not associated with inherited traits account for the other 25% (NMF, 2005).

Epidemiology: Marfan syndrome is one of the more common inherited connective tissue disorders. Marfan syndrome affects about 2 to 3 individuals per 10,000 people (Ammash et al., 2008). Marfan syndrome has a wide range of severity even within families, in which one person might be severely affected and another only slightly. The disorder affects males and females equally and, depending on the severity of the involvement, is diagnosed at birth up to around puberty. It may be found even later for those with minor expression of the disorder.

Pathogenesis: The genetic mutation causes decreased production of fibrillin, a glycoprotein that helps form the extracellular matrices of the connective tissues mentioned above. Without the proper amount of fibrillin, connective tissues are more flexible than they should be, causing abnormal stretching of the various connective tissues, which results in all of the major manifestations of this syndrome.

Extraoral Characteristics: Many think Abraham Lincoln might have had Marfan syndrome because he exhibited all of the associated skeletal characteristics. There are three major categories of manifestations: skeletal, ocular, and cardiovascular. Approximately 88% of individuals affected by Marfan syndrome are very tall and slim and have long arms and legs in relation to their torsos (Fig. 6.18). They usually have very long fingers and toes. Scoliosis or curvature of the spine and either a depressed or protuberant breast bone or sternum is common; their bones, especially rib bones, may be deformed. There is a generalized joint laxness resulting in hyperextensibility and potential injury. The unusual length of the bones and other boney defects are due to an overly flexible periosteum that does not restrict the amount of growth. Joint laxity is due to the increased flexibility of the ligaments.

FIGURE 6.18. **A.** Marfan syndrome. Father, son, and daughter with Marfan syndrome. Father is 38 years old and has had his mitral valve replaced. Daughter is 16 and has had surgery to correct a depressed sternum. Son is 10 and has had surgery to remove an extra toe. **B.** Seven years later. (Courtesy of the Waters family.)

The most common (79%) ocular defect seen in Marfan syndrome is off-center lenses caused by increased flexibility of the ligaments holding them in place. Myopia and cataracts are common problems.

The most serious manifestations of the syndrome are found in the cardiovascular system and include weakness of the aorta and heart valve defects, especially of the mitral valve. About 80% of adults have an enlarged aorta due to structural weakness that can lead to aneurysms (thinning and bulging of the vessel wall) and rupture or dissection of the vessel (see Chapter 8). Eighty percent of children are diagnosed with mitral valve prolapse by the age of 10. Increased elasticity of the muscles controlling the function of the valves cause the valve defects, which can lead to cardiac hypertrophy, dysrhythmia, tachycardia, shortness of breath, and heart failure (Dietz & McKusick, 2009). These are also discussed in Chapter 8.

Perioral and Intraoral Characteristics: The dental problems most commonly observed in Marfan syndrome are related to the development of the bones of the face. The individual may have a high narrow palate, posterior crossbite, and a class II malocclusion. Patients may also have significant crowding of the teeth due to these abnormalities. The temporomandibular joint (TMJ) may be affected by either bone deformity or laxity of the ligaments that control the joint during function. Either of these can cause the individual with Marfan syndrome to be more susceptible to TMJ dysfunction. The presence of a bifid uvula may indicate Loeys-Dietz syndrome (LDS), recently identified to be related to Marfan disorder, which is characterized by aneurysms throughout the arteries of the body, not just the aorta (Fraizer-Bowers, no date).

Distinguishing Characteristics: The most obvious characteristics are those related to the skeletal system: height, length of arms and legs, etc.

Significant Microscopic Features: Not applicable

Dental Implications: Preventive care should be stressed to limit the potential for creating a bacteremia. Dental treatment modifications should include prophylactic antibiotic coverage per American Heart Association recommendations for those with heart valve replacements. Blood tests should be done to determine coagulation status. Regular dental care should be a high priority; patients with Marfan syndrome have no more contraindications for dental care than normal patients with the same type of cardiac or skeletal problems. Patients who are aware of their disorder will most likely know whether cardiac defects exist or not. The problem is the patient who has not been diagnosed. The National Marfan Foundation believes dental professionals should use their knowledge of the physical manifestations of Marfan syndrome to refer patients with symptoms for further medical evaluation. Patients with bifid uvula and other symptoms suggestive of Marfan syndrome that might lead to a diagnosis of LDS should be immediately referred for evaluation and diagnosis (Fraizer-Bowers, no date).

Differential Diagnosis: Not applicable

Treatment and Prognosis: Medical treatment for those with Marfan syndrome centers on anticipating problems, early intervention, and dedicated follow-up. Many skeletal abnormalities including scoliosis can be corrected with physical therapy and braces. Surgery can correct skeletal problems that cannot be prevented or need more aggressive treatment. Ocular defects can usually be treated with glasses and sometimes laser surgery.

Ninety percent of deaths are due to cardiovascular events. Many of these patients are on medication such as beta-blockers to reduce the strength and number of cardiac contractions and to lower blood pressure, thus putting less strain on the aorta. Heart valve involvement is common and many individuals have had valve replacements and will be taking anticoagulants for the rest of their lives.

In 1970, the life expectancy of an individual with Marfan syndrome was approximately 30 to 40 years. This increased in 1995 to about the same as a normal individual, or 72 years. The increase is thought to be due to better medical, surgical, and pharmacologic management and early diagnosis of cardiac problems.

NAME: Cleidocranial dysplasia (CCD)

Etiology: CCD has been determined to be caused by a deletion of genetic material on the short arm of chromosome 6 in region 21 (6p21). The *CBFA1* gene is a core-binding factor that plays a role in osteoblast formation and the differentiation of other cells necessary for normal bone development (Mundlos, 1999).

Method of Transmission: CCD has an autosomal dominant inheritance pattern. About one-third of all cases are caused by a spontaneous mutation not related to inheritance.

Epidemiology: CCD occurs equally in males and females and within all racial and ethnic groups.

Pathogenesis: The *CBFA1* gene controls the differentiation of precursor cells into osteoblasts. Without osteoblasts there is no bone matrix and therefore no bone. All of the characteristics of this disorder are associated with this defect.

Extraoral Characteristics: Individuals with CCD are of moderately short stature and are at risk for skeletal problems such as scoliosis. They have underdeveloped, hypoplastic, or missing clavicles, which allows them to almost bring their shoulders together in front of them (Fig 6.19). Characteristic facial features include enlarged rounding, or **bossing**, of the frontal and parietal bones, caused by delayed closure of the sutures and fontanels. The paranasal sinuses may be missing or hypoplastic, and the nose has a wide nasal root and depressed bridge. Other facial bones are hypoplastic, giving the face a small short look. There may also be a wider distance between the eyes, called **hypertelorism**.

Perioral and Intraoral Characteristics: The most striking intraoral manifestation of this disorder is multiple

FIGURE 6.19. Cleidocranial dysplasia. Extreme hypermobility of the shoulders is secondary to agenesis or hypoplasia of the clavicles. This patient can approximate his shoulders under the chin. (Courtesy of Kenneth E. Yochum, DC, St. Louis, Missouri.)

supernumerary teeth thought to be due to the delayed resorption of the dental lamina, which appears to reactivate when the crowns of the permanent teeth are completely formed (Regezi et al., 2008). While the primary dentition usually develops normally, there is a marked delay in exfoliation and an extreme delay in eruption of the permanent dentition thought to be caused by a lack of cellular cementum on the roots of the teeth, which is characteristic of CCD. The presence of many supernumerary teeth also interferes with the eruption of the permanent dentition (Fig. 6.20). Often patients have an extended period of time when they have few, if any, erupted teeth, known as **pseudoanodontia**. The maxilla is hypoplastic with a high narrow palate, and cleft palate is common. All of these dental anomalies result in severe malocclusion.

Distinguishing Characteristics: The characteristic appearance of individuals with CCD and the presence of multiple supernumerary teeth are distinguishing features of this disorder.

Significant Microscopic Features: Not applicable

Dental Implications: Delayed exfoliation of the primary dentition, delayed eruption of the permanent dentition, and multiple supernumerary teeth result in many dental abnormalities. Dental treatment should start early, and regular dental care should be a lifelong goal. Orthodontic treatment is usually necessary to establish a stable dentition. Temporary full or partial dentures may need to be constructed over unerupted teeth to enable proper function until the teeth erupt. It may be necessary to extract primary teeth and surgically expose unerupted permanent teeth to assist in the eruption process. If clefting is present, corrective surgery is indicated.

Differential Diagnosis: Other disorders that present with delayed exfoliation of primary teeth, delayed eruption of permanent teeth, and multiple supernumerary teeth that might be considered in a differential diagnosis include:

1. Hypothyroidism–Chapter 7. These individuals exhibit delayed eruption of the permanent teeth but do not exhibit the characteristic skeletal features of CCD, and they usually do not present with supernumerary teeth.

FIGURE 6.20. Cleidocranial dysplasia. Panoramic radiograph showing multiple supernumerary and unerupted teeth in addition to retained deciduous teeth. (Courtesy of Dr. N. Lakshmi kavitha Nadendla, Kamineni Institute of Dental Sciences, India.)

2. Cherubism–Chapter 10. Individuals affected by cherubism exhibit delayed eruption of the permanent dentition, but they also present with early exfoliation of the primary dentition, which is not consistent with CCD. They also lack the characteristic skeletal deformities.
3. Gardner syndrome–Chapter 19. Gardner syndrome presents with multiple supernumerary teeth and multiple osteomas. The osteomas are not consistent with a diagnosis of CCD, and these patients do not have the bone abnormalities associated with CCD.

Treatment and Prognosis: The skeletal defects do not usually interfere with the health of the patient and therefore do not need treatment. An exception to this is if the individual develops scoliosis. Children may be advised to wear protective headgear to prevent damage if the fontanels are open. Individuals with CCD have every expectation for a normal life span.

NAME: Treacher Collins syndrome (TCS) (mandibulofacial dysostosis, Treacher Collins-Franceschetti syndrome)

Etiology: A mutation of the *TCOF1* gene on the long arm of chromosome 5, region 32 is believed to be the cause of this syndrome.

Method of Transmission: TCS has an autosomal dominant inheritance pattern with high penetrance and variable expressivity. The disorder becomes more severe as it is passed from generation to generation. About 60% of affected individuals are believed to have had a spontaneous mutation that was not inherited from either parent (U.S. LM, 2006).

Epidemiology: This disorder occurs in about 1 in 50,000 live births, occurs equally in males and females, and affects all ethnic groups (Trainor et al., 2009).

Pathogenesis: The pathogenesis of this syndrome is unknown.

Extraoral Characteristics: The facial features related to TCS are quite striking and have been called birdlike (Fig. 6.21). The eyes slant downward, and the lower lid is notched and missing most or all of the eyelashes. The zygomatic processes, mandible, and maxilla are hypoplastic. Ears are usually low set and malformed, but may be totally missing, and there is always some hearing loss. Residual ear tags can be located anywhere along the line from the commissures to the angle of the mandible. Sideburns may extend onto the cheek in an oblique direction. There are no mental deficits associated with TCS.

Perioral and Intraoral Characteristics: A high vault is normally present, and approximately 30% may have cleft lip and/or palate. All will have mandibular hypoplasia. Severe malocclusion, composed of an open bite, wide interproximal separations, and displaced teeth, is common in patients who have TCS.

FIGURE 6.21. Treacher Collins syndrome or mandibulofacial dysostosis. The face is small, but head size is normal. The eyes slant down, and there are underdeveloped or absent malar bones. The zygomatic arch is evident. Lower eyelids show symmetrical defects in the outer one-third and sparse lashes. Ear deformities and conduction deafness are also normally present. The lower jaw is small and angled downward, giving an open bite malocclusion. This child required tracheostomy to manage severe airway problems caused by micrognathia and incorrect development of the tongue. (From Gold DH, Weingeist TA. Color atlas of the eye in systemic disease. Baltimore: Lippincott Williams & Wilkins, 2001.)

Distinguishing Characteristics: The facial features associated with this disorder distinguish it from other disorders.

Significant Microscopic Findings: Not applicable

Dental Implications: The intraoral and perioral features of this syndrome are significant because collaboration with a team of specialists is needed to successfully treat patients with TCS. Regular dental care including adequate home care instruction is crucial because of the extensive treatment and length of time required to complete the treatment.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment focuses on correcting the facial defects by surgical means and the oral defects by surgery and orthodontics. Hearing aids can assist those with partial hearing loss, and those with total hearing loss may be helped with cochlear implants. Individuals with TCS have every expectation for a normal life expectancy.

NAME: Ehlers-Danlos syndrome (EDS)

Etiology: Genetic defects on chromosomes 1, 2, 6, 9, and 17 have been associated with the different types of EDS.

Method of Transmission: Most forms of EDS follow an autosomal dominant inheritance pattern; fewer show a recessive pattern, and rarely an X-linked pattern is involved.

Epidemiology: The combined frequency of the three most common types of EDS has been estimated at 1 in every 5,000

to 10,000 live births (EDNF, 2010). There is equal distribution of the dominant and recessive types among males and females. The X-linked type is only expressed fully in males.

Pathogenesis: The defects seen in all types of EDS are associated with the production of abnormal collagen and its incorporation into the structures of the body. Collagen is the major structural protein in the body, and use of the defective collagen leads to weakness in structures that are comprised of it.

Extraoral Characteristics: There are more than 10 identified types of EDS. All of the various types present with varying degrees of excessively loose joints that tend to dislocate easily (Fig. 6.22); hyperelastic, thin, loose skin (Fig. 6.23); and excessively fragile skin, mucous membranes, blood vessels, and other body tissues. Wounds often heal abnormally with thin paper-like scarring, especially over bony prominences such as the knees and elbows.

Blood vessels and hollow organs are at risk for rupture causing immediate death. Defective collagen may result in deformed heart valves, the most common of which is mitral valve prolapse. Most individuals with EDS have chronic joint pain and are at higher risk than normal for degenerative bone and joint diseases.

A

B

FIGURE 6.22. Ehlers-Danlos syndrome. **A.** Wrist and thumb hypermobility. **B.** Finger hypermobility with 90-degree bend of the hand. (Courtesy of Veronica Foale, *http://somedaywewillsleep.com/.)*

FIGURE 6.23. Ehlers-Danlos syndrome. Hyperextensible skin. Skin can be stretched over 6 cms. (Courtesy of Veronica Foale, *http://somedaywewillsleep.com/.*)

Perioral and Intraoral Characteristics: Thin hair, deformed ears, hypertelorism, narrow curved nose, and scarring of the forehead and chin may be observed. The TMJ is prone to dislocation and chronic pain. The tongue is unusually supple and most individuals can touch the tip of their nose with the tip of their tongues (**Gorlin sign**); only 8 to 10% of the general population can manage this act (Létourneau et al., 2001). The oral mucosa is fragile and easily torn during eating or dental care. Gingival tissues can be hyperplastic and often bleed easily during home care, even without inflammation. Teeth may be malformed, with deep occlusal grooves and higher-than-normal cusps. The roots may be short and/or dilacerated, and the dentin and enamel structure may be abnormal.

Distinguishing Characteristics: Skin hyperelasticity, joint hypermobility, and excessive bruising are all distinguishing characteristics of this disorder.

Significant Microscopic Features: Not applicable

Dental Implications: In all types, mucous membrane fragility, poor wound healing, and joint hypermobility could require treatment modifications. Dental treatment should focus on providing optimum care without trauma. Short appointments should be scheduled to avoid damaging the TMJ. The need for surgical procedures should be determined on the basis of anticipated benefits versus the risks of bleeding and inadequate wound healing. Any sutures should be protected by acrylic splints or periodontal dressings to help avoid tearing of the tissues. Excellent home care should be stressed to decrease the risk of periodontal disease and to decrease the risk of infective endocarditis in susceptible individuals. Orthodontic treatment is still possible, but forces should be adjusted to account for faster movement of the teeth. The retention phase needs to be extended to reduce the chance for relapse due to greater periodontal ligament elasticity.

Differential Diagnosis: Not applicable

Treatment and Prognosis: General treatment for EDS depends on the type and severity of the disorder. Orthopedic braces help to stabilize joints. A special type of finger brace that looks like jewelry can help keep the knuckle joints from collapsing as the person is writing or doing other work requiring fine finger motion. Individuals should be cautioned about participating in activities that would put too much stress on the joints. One of the most severe forms of the disorder, the vascular form, has the potential for causing death before the age of 40 due to organ rupture or large vessel rupture. Those with other types of EDS have relatively normal life expectancies (Létourneau et al., 2001).

NAME: Papillon-Lefèvre syndrome (PLS) (palmoplantar keratosis [PPK] with periodontitis)

Etiology: PLS is associated with a group of disorders with various forms including genetic and acquired. PLS has a genetic origin. It can be traced to a gene called Cathepsin C on the long arm of chromosome 11q14-21.

Method of Transmission: PLS has an autosomal recessive inheritance pattern.

Epidemiology: PLS is a rare disease, occurring more often in children of consanguineous parents, such as a union between first cousins. PLS occurs in about 1 of 250,000 to 1,000,000 births. The disorder affects all ethnic groups and males and females equally.

Pathogenesis: The pathogenesis of PLS is not well understood, partly because of the infrequency of its occurrence and partly because it is often misdiagnosed. Current research tends to point to defective chemotactic and phagocytic functions in neutrophils and/or a T lymphocyte defect, but the results of these studies are not consistent (Lundgren et al., 2005). In a recent study, the numbers of natural killer (NK) cells were found to be consistently and severely depressed in the subjects tested (Lundgren et al., 2005). Whatever the mechanism, the outcome is severe, with aggressive periodontal disease resulting in loss of both dentitions.

Extraoral Characteristics: The major feature is hyperkeratosis comprising scaly red lesions on the palms of the hands and the soles of the feet (Fig. 6.24) and possibly over joints such as the knees and elbows. The individual may exhibit excessive sweating, or **hyperhidrosis,** with associated malodor. There may be increased susceptibility to chronic and recurrent infections such as colds, ear infections, and skin infections.

Perioral and Intraoral Characteristics: Intraoral symptoms do not appear until the first tooth has erupted. A short time after eruption, signs of gingival inflammation appear and become progressively worse, resulting in periodontal attachment loss. Loss of alveolar bone and deep pocket formation consistent with severe periodontal disease are present (Fig. 6.25). Primary teeth are normally all lost by age 5 after which the gingiva returns to normal. Permanent teeth erupt at the appropriate time, and the symptoms appear again. Children with PLS usually lose all permanent teeth before the age of 15. Some research has identified an increased number of *Actinobacillus actinomycetemcomitans* (AA) and other periodontal pathogens in the subgingival area, which implies a possible immune deficiency.

FIGURE 6.24. Papillon-Lefèvre syndrome. Palms of the patient in Figure 6.25 showing the diffuse erythematous hyperkeratosis, scaling, and fissuring characteristic of this disorder. (Courtesy of Dr. Faiez N. Hattab.)

Distinguishing Characteristics: The anatomic location of the hyperkeratotic lesions and the associated severe periodontal disease are the distinguishing features of this disorder.

Significant Microscopic Features: White blood cell counts, specifically neutrophils and NK cells, may be decreased.

Dental Implications: Severe periodontal disease in a child is almost unheard of, and if a child does present with this disease, PLS should be considered immediately. Simple observation of the palms of the hands can reveal the other significant feature of this syndrome, hyperkeratosis, which is often misdiagnosed as eczema.

FIGURE 6.25. Papillon-Lefèvre syndrome. Intraoral view showing generalized severe inflamed and swollen gingiva around the remaining teeth. All primary teeth have been lost prematurely in this 9-year-old girl with Papillon-Lefèvre syndrome. (Courtesy of Dr. Faiez N. Hattab.)

Differential Diagnosis: A group of syndromes has PPK as part of their clinical manifestations; however, PLS is the only one associated with severe periodontal disease. Other diseases that manifest with severe periodontal infection should be considered, including:

1. Hypophosphatasia–Chapter 21. An autosomal recessive disorder causing a deficiency of alkaline phosphatase essential in the maintenance of bone and one of the few disorders that cause early exfoliation of the primary dentition. The structure of the tooth, not a periodontal infection, is the problem and only the primary dentition is usually involved. There is no associated PPK.
2. Cyclic neutropenia–Chapter 9. A periodic decrease in the number of neutrophils in the blood and marrow occurring about every 21 days that leaves individuals prone to many infections, including periodontal disease. Blood tests to determine the levels of neutrophils present at different times over a period will help to differentiate this disorder from PLS. There is no associated hyperkeratosis.
3. EDS with periodontitis–Chapter 6. EDS with periodontitis can exhibit the same type of severe periodontal disease with complete loss of permanent teeth as PLS, but PLS would not exhibit the skin hyperelasticity seen in EDS. The oral tissues and blood vessels are not fragile in PLS.

Treatment and Prognosis: Treatment for hyperkeratosis consists of oral and possibly topical retinoids, a derivative of vitamin A used to treat severe acne and psoriasis, and sometimes mechanical exfoliation of the scaly lesions (Lee et al., 2011). Treatment for the periodontal disease focuses on extracting hopeless teeth and eventually full dentures. One recent study found with diligent home care and professional supervision it may be possible to maintain the dentition of those affected by PLS much longer than was ever thought possible (Lundgren & Renvert, 2004). The medical prognosis for individuals with PLS is the same as the general population.

NAME: Gingival fibromatosis

Gingival fibromatosis is included in the clinical manifestations of more than a few syndromes and disorders. It is outside the scope of this text to discuss all of these. Table 6.4 presents an overview of the disorders seen in association with gingival fibromatosis. This section discusses hereditary gingival fibromatosis as a separate entity, the clinical aspects of which are consistent with most of these other disorders.

APPLICATION 6.3

Could this be Genetic?

Imagine one day you are working and come across a patient who exhibits a particular clinical finding that makes you wonder if inheritance or genetics influenced its development. Where would you begin to research this possibility? The Web site Online Mendelian Inheritance in Man (OMIM) has the information you need. Go to the Web site (it is listed in the Media Menu at the end of this chapter) and follow the steps below:

1. Enter terms describing the clinical manifestation you are researching in the search box, for example, "enamel defect" AND "delayed eruption" (Boolean phrases should be all uppercase letters). If you are unsure of how to write in your search terms, click the "Help" link at the top of the page and select "Search Help" from the drop-down menu. You can also access sample searches by clicking on "Sample Searches" to the right of the "Search" button.
2. After you have entered your search terms, click "Search" to view a listing of all of the conditions in OMIM associated with the search parameters. In our sample search for "enamel defect" AND "delayed eruption" there is only one match: otodental dysplasia. Most often there will be a list of potential matches and you will need to go through them individually or refine your search terms to reduce the number of listed conditions.
3. The name of the condition is an active link; click on this link. This will bring up a page with information about the condition, including: alternative titles and symbols, a list of other entities represented in the entry, gene phenotype relationships, and a link to the clinical synopsis. The text found under this information contains a description of the condition, clinical features, mapping, molecular genetics, and references for the information on the page.
4. Click on the "Clinical Synopsis" link after the Gene Phenotype Relationships table to view a concise listing of the pertinent clinical features.
5. In the right-hand menu bar, you will find a "Table of Contents" and External Links. To learn more about the disorder you have been researching, click on "Clinical Resources" and choose any of the links. OrphaNet is a favorite site for finding information on rare diseases and orphan drugs. Others include the following:
   - Clinical Trials—A registry of federally and privately supported clinical trials conducted in the United States and around the world.
   - Gene Tests—Information on genetic testing and its use in diagnosis, management, and genetic counseling.
   - Genetic Alliance—Network of disease-specific advocacy organizations, universities, private companies, government agencies, and public policy organizations.
   - POSSUM—A dysmorphology database of multiple malformations; metabolic, teratogenic, chromosomal, and skeletal syndromes; and related images. This site requires a paid annual subscription.

Dentists and dental hygienists are the appropriate health care professionals to identify many clinical entities suggestive of an inherited trait. Approximately 40% of the diagnostic criteria for genetic conditions involve the head and neck and many are limited to oral structures (NCHPEG, About the Program, Genetics, Disease and Dentistry, 2011). In light of this, it is important that dental professionals be alert to a potential genetic basis for conditions in the oral and head and neck regions. Dental professionals should know how to research these conditions and refer patients for appropriate genetic counseling or services.

TABLE 6.4 Disorders Associated with Gingival Fibromatosis

These are selected examples of a variety of conditions that may present with gingival fibromatosis as one of their elements.

Name	Etiology	Characteristics in Addition to Gingival Fibromatosis
GF[a] with progressive deafness	Unknown	Deafness
GF with hypertrichosis	Autosomal dominant	Excessive hairiness usually on the back and limbs
Zimmerman-Laband syndrome	Autosomal dominant	Structural ear abnormalities, deformed and hypoplastic nails, short fingers, excessive hairiness; delayed tooth eruption and high-arched palate; hepatosplenomegaly[b]
GF with distinctive facies	Autosomal recessive	Large head, bushy eyebrows, hypertelorism, downslanting eyes, flat bridge of nose, and high arched palate
Ramon syndrome	Autosomal recessive	Cherubism,[c] epilepsy, mental retardation, hypertrichosis, stunted growth, eye abnormalities
Juvenile hyaline fibromatosis	Autosomal recessive	Nodular and papular skin growths on the hands, scalp, and ears and around nose; joint contractures;[d] osteopenia[e]
Infantile systemic hyalinosis	Autosomal recessive	Joint contractures; red hyperpigmentation over prominent bones; papular and nodular growth on face, scalp, neck and perianal areas; thick skin; osteopenia
Rutherford syndrome	Autosomal recessive	Abnormalities of the cornea and delayed primary tooth eruption and failure of secondary teeth to erupt

[a]GF, gingival fibromatosis.
[b]Enlarged spleen and liver.
[c]See Chapter 10.
[d]Painful stiffness in a flexed position.
[e]Lower than normal mineral content in the bones but not enough to be considered osteoporotic.

Etiology: Gingival fibromatosis has been associated with genes located on chromosomes 2 and 5.

Method of Transmission: Both autosomal dominant and autosomal recessive inheritance patterns have been observed.

Epidemiology: Unknown

Pathogenesis: Gingival fibromatosis is a slow and progressive collagenous overgrowth of the fibrous connective tissue of the gingiva. It does not normally occur prior to the eruption of teeth.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: Gingival fibromatosis can occur in a generalized or localized form. The maxillary arch is more common than the mandible, and posterior areas are more common than anterior areas. Enlargement can begin at any time but normally occurs with eruption of the deciduous teeth and rarely occurs for the first time after age 20. The tissue can grow over the crowns of the affected teeth and can cause failure or delayed eruption of permanent teeth (Fig. 6.26). The tissue appears normal in color and is firm to the touch. The posterior palatal area is often involved, with the gingival overgrowth almost covering the crowns of the teeth and extending toward the midline of the palate, almost touching in some cases. Gingival overgrowth will stop if the patient becomes edentulous.

Distinguishing Characteristics: Hereditary forms of gingival fibromatosis usually present as symmetrical gingival enlargements comprising normal-appearing tissues. This observation may help to distinguish this from other forms of gingival enlargement, such as the enlargement associated with phenytoin, a medication used to treat seizures, and that associated with gingivitis.

Significant Microscopic Features: Microscopic examination will show dense collagenous tissue with long thin rete ridges that run deep into the connective tissue.

Dental Implications: Rule out any syndromes associated with gingival fibromatosis and develop treatment and home care plans that can help the individual overcome the difficulties associated with this disorder.

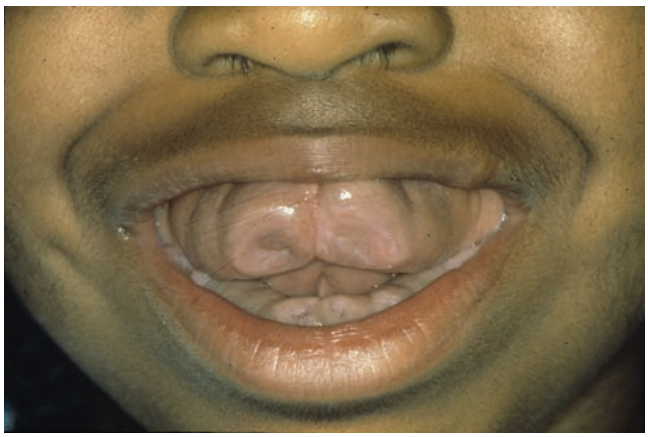


FIGURE 6.26. Hereditary gingival fibromatosis. Note the thick, normal-colored gingiva enveloping the teeth. The treatment is surgical removal of the excess gingiva, but it always recurs. (Courtesy of Dr. Charles Dunlap.)

Differential Diagnosis: Gingival hyperplasia due to hormones, medications, and local factors must be considered in a differential diagnosis of gingival enlargement (see Chapter 17). The medical history is very important in ruling out medication-induced hyperplasia and hyperplasia due to pregnancy. Even without the medical history information, there are clinically observable differences in these entities. Hyperplasia due to hormonal influences and local factors such as dental biofilm is usually erythematous, spongy, and bleeds easily. Medication-induced hyperplasia has a very pebbly appearance and is usually firm to the touch.

Treatment and Prognosis: Surgical removal of the excess tissue may be the only way to attempt to control the symptoms. The gingiva usually continues to grow and multiple surgeries are necessary during the life of the individual. Erupting teeth may need to be "helped" through the thick gingival tissues with surgical crown exposure techniques.

In both localized and generalized forms, it is very important to maintain excellent oral hygiene because inflammation from infection will exacerbate the growth of tissue. Dental hygienists have an opportunity to help patients develop home care regimens that are effective and make compliance as easy as possible. More frequent preventive care appointments are strongly suggested to assist in maintaining healthy tissues.

NAME: Ectodermal dysplasia (ED)

There are over 150 different inherited syndromes associated with ectodermal dysplasia. They follow all inheritance patterns and manifest in a full range of severities. Mutations and deletions associated with ED syndromes have been mapped to the X chromosome and chromosomes 9, 12, 13, and 19. Worldwide, ectodermal dysplasia syndromes occur in about 7 of every 10,000 births. Males and females of all ethnic groups are equally affected by these syndromes, even though several are X-linked. The following discussion focuses on the most common form of ED, X-linked hypohidrotic ectodermal dysplasia (EDA).

Etiology: EDA is linked to a mutation of the *ED1* gene on the X chromosome.

Method of Transmission: EDA follows an X-linked recessive inheritance pattern, so only the male will exhibit the complete phenotype. There have been reports of an intermediate expression of the disorder in some heterozygous females (OMIM 305100, 2009). Females only exhibit the full disease if the parents were an affected male and a carrier female.

Epidemiology: The estimated prevalence of EDA in the United States is 1 in 100,000 births. While all races may be affected, ED syndromes appear to occur more often in whites (Shah, 2009).

Pathogenesis: The clinical manifestations of EDA are the result of abnormal morphogenesis of the tissues that develop from the embryonic ectodermal cells. This includes skin, mucous membranes and associated glands of the oral cavity and upper respiratory system, sweat glands, hair follicles, and hair, nails, and teeth.

Extraoral Characteristics: The typical expression involves sparse or missing hair (entire body), hair and hair follicle defects, absent or few sweat glands, defective mucous glands, and lacrimal gland defects. The skin is thin, smooth, and dry, with a shiny appearance. Characteristic facial features include frontal bossing, midface or maxillary hypoplasia, flattened bridge of the nose or saddle nose, and wrinkled hyperpigmented skin around the eyes. The ears can be large and low set. The nails are normal in EDA. See Chapter 21 for a picture of the characteristic facial features. The lack of adequate numbers of, or total absence of, sweat glands results in a tendency for high fevers or pyrexia and hyperthermia due to an inability to regulate body temperature. Temperature regulation is especially difficult for infants and children and frequent bouts of hyperthermia can cause seizures, brain damage, and even death. Individuals with EDA are more susceptible to severe and recurrent respiratory infections due to a decreased amount of respiratory secretions and the existence of defective respiratory secretions which are believed to impair the host response. Defective lacrimal glands cause **xerophthalmia** (dry eyes) and associated **photophobia** (light sensitivity).

Perioral and Intraoral Characteristics: Individuals with EDA have thick full lips. Intraoral problems include **anodontia** (missing all teeth) or **hypodontia** (missing some teeth) with hypoplasia and varying degrees of xerostomia. Hypodontia is more common than anodontia. See Chapter 21 for examples of hypodontia associated with ED. Tooth eruption is delayed and teeth are usually small and conical. Cleft lip and/or palate are not a component of this syndrome but are seen in other ED syndromes.

Distinguishing Characteristics: One of the difficulties associated with EDA is the relative lack of clinical manifestations in newborns and older infants. EDA diagnosis is often made when the infant has recurrent problems with pyrexia. In older children and adults, the lack of hair and the dental abnormalities seen with this disorder are distinguishing characteristics.

Significant Microscopic Features: Not applicable

Dental Implications: Dental abnormalities and severe xerostomia are the most significant factors for dentistry. Missing teeth can be replaced with prosthetic appliances or implants. Hypoplastic teeth can be esthetically restored. Xerostomia increases the likelihood for dental biofilm accumulation and increased caries activity and makes prosthetic appliances more difficult to use and care for. Home care procedures are complicated by the type and number of restorations and prosthetic appliances. Xerostomia can be alleviated with artificial saliva, mechanical stimulation with sugarless gum or candies, and medication, if indicated. Adequate oral hygiene is essential and the dental hygienist will be responsible for developing user-friendly home care

regimens. Fluoride treatments in the office and at home will be crucial to inhibit caries activity.

Differential Diagnosis: Other ectodermal dysplasia syndromes need to be ruled out as well as any condition that causes anodontia or hypodontia. Other conditions that might cause anodontia or hypodontia are relatively easy to rule out because of the other elements of the syndrome. However, if a heterozygous female without the classic elements of ED presented with hypodontia of the type seen in this disorder, identification of the problem might be more difficult.

Treatment and Prognosis: There is no treatment for this syndrome, however, the symptoms can be treated and corrected. No matter how problematic sweating is for most of the human race, it does serve a purpose. Individuals with ED have to learn how to maintain a proper temperature, including what type of clothing to wear; avoiding activities that increase temperature; regulation of home, work, and school environments; and proper hydration. Xerophthalmia and photophobia can be relieved with artificial tears and ointments.

Patients who survive early childhood have a relatively normal life expectancy. Infants and young children have an approximate mortality rate of 30% for all of the ED syndromes, not just EDA. The most frequent causes of death are associated with the sequela of hyperthermia such as seizures and brain damage (Shah, 2009; OMIM 305100, 2009).

Multifactorial Inheritance

Multifactorial inheritance describes a process that reflects the additive effects of a number of genes and environmental factors. Most of our makeup is not determined by the influence of a single gene or even multiple genes, but by the interaction of many genes and the environment. The environment plays a very important role in determining the full expression of our genetic potential. Someone who inherits above-average intelligence but is not exposed to anything but a dark room will not develop to his or her potential. Likewise a boy who grows up with chronic malnutrition will not achieve the 6-ft height he inherited from his grandfather. The mechanisms of inheritance discussed thus far are relatively simple; however, most genetic disorders do not follow a simple pattern of inheritance. Many disorders require an environmental trigger or exposure to initiate their expression. Cancer is an example of multifactorial inheritance. A combination of environmental, biologic, and genetic events must occur over time before cancer develops, even though an individual may have a defective tumor suppressor gene or may have developed certain oncogenes. Refer to Box 6.6 for a listing of common disorders considered to be multifactorial. One of the most devastating orofacial disorders associated with multifactorial inheritance is cleft lip and/or palate.

BOX 6.6 Multifactorial Inheritance

Examples of disorders commonly considered to be caused by multifactorial inheritance

Adults

Hypertension
Atherosclerosis
Type II diabetes
Psoriasis
Schizophrenia
Ankylosing spondylitis
Gout
Cancer
Obesity
Osteoporosis
Parkinson disease
Alcoholism

Children

Pyloric stenosis
Cleft lip and palate
Congenital heart disease
Congenital hip dislocation

NAME: Cleft lip and/or palate

Etiology: Cleft lip, cleft palate, and the combination of cleft lip and palate are considered to have a multifactorial cause, including both environmental and genetic elements. Oral clefts have been linked to genes located on almost every chromosome (1–4, 6–8, 11, 13–14, 16–17, 19–20, X) (OMIM, 2011). Other genes are thought to either interfere with the clefting process or enhance it. More than 150 different syndromes have cleft lip and/or palate as possible features, accounting for only 1 to 5% of cases. Ten to fifteen percent of cases may be passed from one generation to another depending on environmental factors. Otherwise, the etiology for 75 to 80% of clefts (isolated or nonsyndromic clefts) is not fully understood at this time (OMIM 119530, 2011) and are thought to rely on a combination of genetic and environmental factors. Clefting has been shown to have a possible association with maternal smoking (especially more than 20 cigarettes per day) and exposure to secondhand smoke, but not with paternal smoking (Shaw et al., 1996). Accutane (the drug used to treat severe cystic acne), anticonvulsants such as phenytoin, warfarin (an anticoagulant), and ethanol (the alcohol in beverages) are known to cause clefting and other craniofacial defects (Czeizel, 2000). Studies have now shown a maternal folic acid deficiency contributes to clefting defects. Folic acid has been shown to help prevent neural tube defects such as spina bifida (Czeizel, 2000) and orofacial clefting (Wilcox et al., 2007; Elavenil et al., 2010).

Method of Transmission: The method of transmission depends on the specific cause of the clefting. Multifactorial clefts can exhibit evidence of autosomal dominant, autosomal recessive, and sex-linked inheritance patterns, or they may be the result of a spontaneous mutation or mutations in one or more genes. While genetic factors appear to predispose an individual for clefting, environmental factors act as a trigger to cause development of the cleft.

Epidemiology: Orofacial clefting of some type occurs in approximately 1 of every 500 to 550 live births in the United States. The frequency and cause of oral clefting is highly related to the sex of the individual and the type of cleft involved. Females with a bilateral cleft have the greatest number of genetic influences and the lowest number of environmental factors, and males with a unilateral cleft have the lowest number of genetic influences and the highest number of environmental factors (Tolarova, 2009).

Pathogenesis: Cleft lip/palate occurs when there is incomplete or no fusion of the palate, premaxilla, and related soft tissues during the 6th to 8th week of embryologic development. Multifactorial inheritance implies that changing something in the environment will either interfere with the development of a cleft or enhance the probability a genetic predisposition will result in clefting.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: Refer to Figure 6.27 for examples of cleft lip, cleft palate, and cleft lip and palate. Clefting can interfere with proper development of the teeth and alveolar ridges, causing hypodontia, malformed teeth, bony defects of the maxillary alveolar process, and malocclusion.

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: The dental implications of cleft lip and/or palate depend on the number of dental abnormalities present and the stage of treatment. Dental hygienists play an important role in managing patients with a cleft lip and/or palate through education and preventive dental hygiene therapy.

Up to 70% of neural tube defects (March of Dimes, 2010) and a "significant reduction" in cleft lip and/or palate (Czeizel, 2000) could be prevented by folic acid. Because many women are not aware they are pregnant until after the 12th week, all women of childbearing age not actively preventing pregnancy should eat a diet rich in all nutrients, especially folic acid, and take a multivitamin supplement that contains an appropriate amount of folic acid, approximately 0.4 mg for most pregnancies, significantly more for women who already have a child born with cleft lip and/or palate (Czeizel, 2000). The dental hygienist can help many families by educating patients about this simple preventive action.

Differential Diagnosis: A cleft lip or palate is either present or not present. However, since 10 to 20% of clefts are part of a syndrome, it is important to rule out the presence of these syndromes (refer to Table 6.5).

Treatment and Prognosis: Treatment for cleft palate focuses on prevention first as stated above. Numerous surgical and other medical and dental treatments are necessary to correct cleft lip/palate. The surgeries are scheduled starting at about 3 months of age and ending at about 1 year to correct simple clefts (Fig. 6.28). Orthodontic treatment starts

FIGURE 6.27. Oral clefting. **A.** Bilateral cleft of the lip and palate. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.) **B.** Cleft of the hard and soft palates. (Courtesy of R Chase.) **C.** Unilateral cleft of the upper lip. (Courtesy of R Chase.)

TABLE 6.5 **Inherited Syndromes Associated with Possible Cleft Lip and/or Palate**

Syndrome	Characteristics in Addition to Cleft Lip and/or Palate
Pierre-Robin sequence	Micrognathia Posterior soft palate cleft is more likely than any other type Tongue tends to fall back in the throat Feeding and respiratory problems
Craniofacial dysostosis (Crouzon syndrome)	Abnormal head shape Hypoplastic midface Hearing and vision deficits Severe maxillary hypoplasia and malocclusion
Deletion 22q11 syndrome (DiGeorge sequence)	Congenital heart defects Unique hypoplastic facial features Microcephaly Learning disabilities Thymic hypoplasia
Opitz syndrome	Facial abnormalities Hypertelorism Intellectual defects
Stickler syndrome	Cataracts Midface hypoplasia Hearing loss Hypermobile joints
Saethre-Chotzen syndrome	Early fusion of the skull bones Facial abnormalities Short, webbed fingers and toes Small ears with hearing loss Bone abnormalities
Van der Woude syndrome	Lower congenital lip pits
Cri-du-chat syndrome	Improper development of larynx causing "cat-like" mewing cry Cardiac defects Abnormal thymus gland development Hypertelorism, epicanthal folds Micrognathia (mandible) Delayed eruption and small teeth

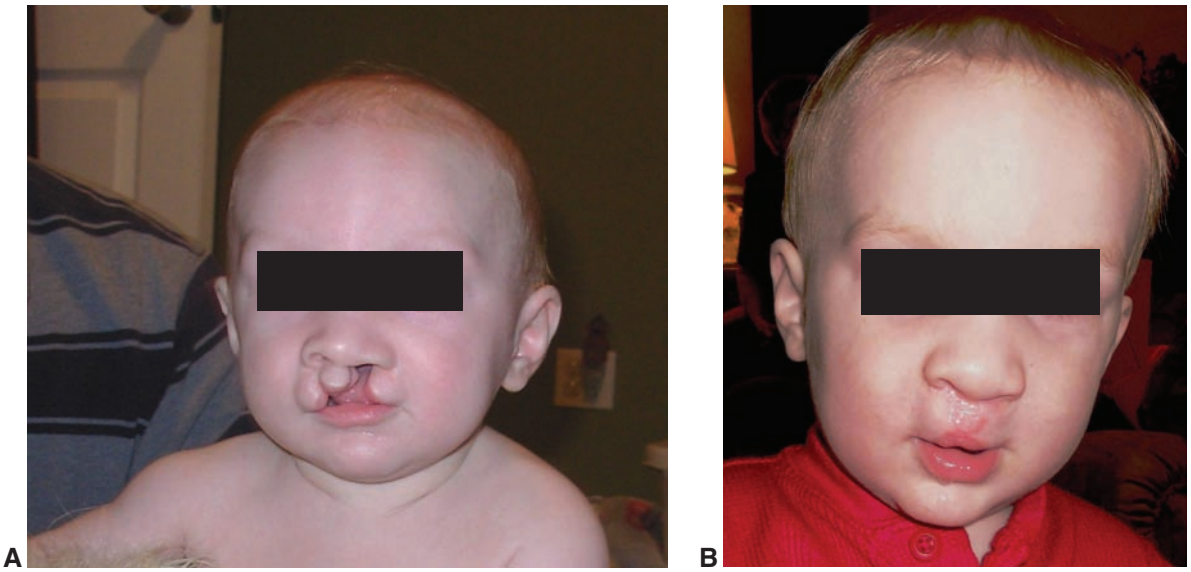


FIGURE 6.28. A. Cleft lip and palate prior to surgery to correct the cleft lip. **B.** Same child 1 year after repair of the cleft lip. Surgery to repair the cleft palate is still pending. (Courtesy of Paula Stidivent, RDH.)

as early as age 1 and continues until all teeth are erupted and into the teen years. Other procedures might include an alveolar bone graft and procedures to correct any nasal deformities (Tolarova, 2009). The prognosis for individuals with a repaired cleft is excellent. Unrepaired clefts can cause eating, speech, and respiratory difficulties along with severe psychologic and social problems.

SUMMARY

- The etiology of most congenital abnormalities is unknown.
- Teratogens cause errors in morphogenesis when an embryo or fetus is exposed to them at a crucial time in organ development. Exposure of the embryo or fetus to teratogenic agents after the 12th week of gestation is much less likely to result in the development of abnormalities.
- FASD are a group of defects associated with the ingestion of alcohol during pregnancy. The amount of alcohol that will cause any of these disorders is unknown and is different for each woman. A diagnosis of FAS requires three criteria be met: growth problems, neurodevelopmental problems, and characteristic facial features. Prophylactic antibiotics might be necessary prior to dental care because these patients have an increased risk of heart defects.
- TORCH syndrome is caused by a variety of organisms that affect the developing embryo/fetus in the womb. The general characteristics include heart defects, mental deficiencies, hearing and vision defects, and premature birth. Oral defects associated with TORCH are related to the specific cause and can include oral clefts and abnormally shaped teeth. Prophylactic antibiotics might be necessary prior to dental care because these patients have an increased risk of heart defects.
- Health care professionals are responsible for integrating genetic information into their practices.
- Genetic material (chromatin) is found in the nucleus of cells and is passed from parents to offspring in the form of chromosomes.
- The structure of each chromosome is unique to that specific chromosome, but each chromosome is made up of a p-arm and a q-arm, a centromere, and two telomeres.
- There are 22 pairs of autosomal chromosomes and 1 pair of sex chromosomes in a diploid cell; haploid cells contain only one of each chromosome.
- Chromosomal crossover is one mechanism to ensure genetic diversity. It occurs during prophase 1 of meiosis at points where sister chromatids touch (chiasma) and exchange genetic information.
- The Lyon hypothesis states genetic material on the second X chromosome in females is largely inactivated to equalize the genetic activity potential between males who have only one X chromosome and females. The inactive X chromosome material can be seen as the Barr body, lying adjacent to the inner surface of the nuclear membrane.
- An individual's genotype is not necessarily expressed in their phenotype because of the characteristics of inheritance; for example, dominance, codominance, mosaicism, and variable expressivity.
- Chromosomal abnormalities involve either the number of chromosomes or their structure.
- Trisomy 21 is usually caused by the nondisjunction of chromosome 21 during meiosis. Trisomy 21 causes mental impairment, congenital heart defects, compromised immune system, hearing and vision defects, and other organ/system defects. Flat facial features and epicanthal folds are characteristic of this disorder. There is a myriad of oral problems associated with trisomy 21, including midface hypoplasia, clefts, malocclusion, and a very high risk of periodontal disease. Prophylactic antibiotics might be necessary prior to dental care because these patients have an increased risk of heart defects.
- Klinefelter syndrome is caused by one or more extra X chromosomes in a male genotype. The individual is male but lacks development of secondary sexual characteristics. Mental deficiencies and learning disabilities are seen more often in those who have more than one extra X chromosome. Congenital heart defects such as mitral valve prolapse are common, indicating the possible need for antibiotic prophylaxis.
- Turner syndrome is the only monosomy that is compatible with life. Individuals with Turner syndrome are very short, have a webbed neck, and do not develop secondary sex characteristics. They usually are of average intelligence but may have learning disabilities. Osteoporosis and endocrine disorders as well as a slightly higher risk of heart and vascular defects are characteristic of Turner syndrome. Prophylactic antibiotics might be necessary prior to dental care because these patients have an increased risk of heart defects.
- Single-gene disorders usually result in the creation of abnormal proteins or the absence of an important protein.
- Single-gene disorders follow dominant, recessive, or sex-linked inheritance patterns.
- Most traits observed in a phenotype are not linked to one gene but are influenced by several genes working together or oligogenic inheritance.
- Marfan syndrome is an autosomal dominant disorder that causes the production of a defective protein that is essential in making certain connective tissues such as the periosteum and heart and vascular tissues. These patients are very tall and have long arms and legs. Mitral valve prolapse is very common, and many individuals have to have the valve replaced. Dental implications include prophylactic antibiotics (if needed), care of the TMJ, and malocclusion caused by a high arched palate.
- CCD is an autosomal dominant disorder causing bone malformation and agenesis. Multiple supernumerary

teeth and delayed eruption as well as pseudoanodontia are common.

- TCS is an autosomal dominant disorder that affects the development of the craniofacial structures, causing gross deformities. There are no other organs or tissues involved, and intelligence is normal. There is always some hearing loss.
- EDS is usually caused by autosomal dominant inheritance. EDS causes the production of an abnormal collagen leading to weakness in the structures that are composed of it. Hyperelastic, thin, loose skin is the characteristic feature of this disorder. Blood vessels, skin, and mucous membranes are very fragile and can be the cause of excessive bleeding after minor trauma. Prophylactic antibiotics might be necessary prior to dental care because these patients have an increased risk of heart defects.
- PLS follows an autosomal recessive inheritance pattern and is associated with severe periodontal disease resulting in the loss of both the primary and permanent teeth several years after they erupt.
- Hereditary forms of gingival fibromatosis are associated with a variety of disorders.
- Forms of ectodermal dysplasia are associated with all types of inheritance patterns. EDA follows an X-linked recessive pattern and is the most common form. The disorder causes the development of defective tissues that are derived from the embryonic ectodermal cells. This includes skin, sweat glands, salivary glands, hair, nails, and teeth. Temperature regulation, increased incidence of respiratory infections, and photophobia are all characteristic of the disorder. Dental implications include hypodontia or anodontia, and xerostomia.
- Multifactorial inheritance involves the additive effects of a number of genes and environmental factors.
- Cleft lip or palate follows a multifactorial inheritance pattern. They have been associated with numerous genetic syndromes and follow any of the inheritance patterns. Most cases are of unknown origin; however, maternal smoking, alcohol, and certain drugs have been associated with cleft development. In addition, folic acid deficiency may be associated with clefts, indicating the possible need for folic acid supplements prior to and during pregnancy.

CHAPTER REVIEW

Case Study 6.1

A 5-year-old child is brought to the dental office for a preventive dental hygiene appointment. The medical history is unremarkable, with no systemic problems noted except the child had to be brought to the hospital more than a dozen times for very high temperatures. The extraoral examination notes pale thin skin with sparse, fine, blond hair. Intraorally, the hygienist notes 10 primary and 11 permanent teeth are missing (Fig. 6.29). The teeth present are small and appear to be shaped abnormally. The maxillary incisors have been restored with composite to disguise their abnormal shape.

1. What additional information would you like to know from the parent?
2. What disorders cause delayed eruption and/or hypoplastic teeth?
3. What disorder do you think this child has?
4. Describe the dental problems related to this genetic disorder.

For answers and additional review activities, log in to **thePoint.lww.com**

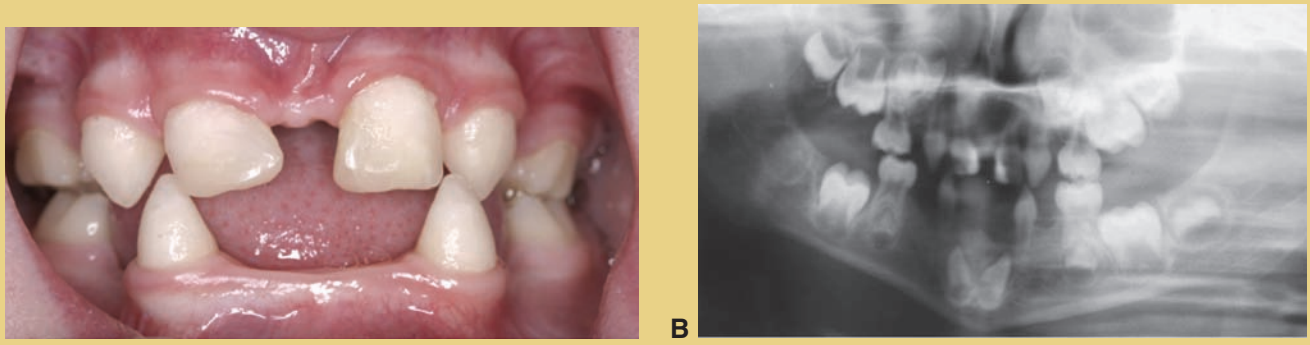


FIGURE 6.29. (From Lind, 2006. See References for complete citation.)

Case Study 6.2

Your next patient is Kaylee, the little girl you see in this picture (Fig. 6.30). She has been playing quietly with a pencil and pad of paper while you have performed periodontal debridement on her mother. Kaylee is 8 years old but has the mental age of a 3- or 4-year-old child.

1. Describe the facial features you observe.
2. What genetic disorder does Kaylee have?
3. What characteristic oral features do you expect to see when you look inside Kaylee's mouth?
4. What education topics should you discuss with her mother?
5. What oral problems can Kaylee expect as she grows into adulthood?

FIGURE 6.30. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

For answers and additional review activities, log in to **thePoint.lww.com**

Critical Thinking Activities

1. Extra X chromosomes are found in Klinefelter syndrome; Turner syndrome is caused by the loss of an X chromosome. Why is there no mention of a syndrome that is characterized by a missing Y chromosome?
2. Why must all carriers of recessive traits be heterozygous for those traits?
3. Describe the mechanisms that can modify the phenotypic expression of an individual with a particular genotype. Why doesn't everyone with a particular genotype exhibit the exact same characteristics?
4. When you look at all of the genetic disorders discussed what do you feel are the most important dental/medical concerns that you will be faced with when determining dental hygiene care for these individuals? Why?
5. How do you feel genetic concepts should be incorporated into the practice of dentistry and dental hygiene? What should the role of the dental hygienist or dentist be?

Portfolio Possibilities

- Get involved with Special Olympics: offer to present an educational session on basic oral hygiene care or help to perform the dental examinations that they offer for the participants. Make sure to get pictures of your adventure and write a summary of your experiences reflecting on what you have learned and how dental hygienists could make a difference in this population.
- Visit the Web page of an organization offering support to patients with a disorder that interests you. Contact the organization and offer to answer questions on basic oral hygiene care to visitors to the site. You can also offer to research more complex questions or find an appropriate referral for them. Another option would be to ask visitors to the site what their dental experiences have been: Do they have a problem with access to care? Have the problems associated with their disorder been adequately addressed? Do they have specific needs that have not been addressed? Include copies of your correspondence with these individuals (identifying information blocked out) in your portfolio, with a reflection of your thoughts on what transpired and what the dental hygiene profession might do to improve services to patients with this disorder.

Media Menu

Web Sites

The Merck Manual for Healthcare Professionals (free online access), excellent reference for all medical and dental topics:
http://www.merckmanuals.com/professional/index.html

Orphanet: Portal for rare diseases and orphan drugs:
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=EN&Expert=281

UNSW Embryology: Information and pictures related to normal embryological and fetal development:
http://php.med.unsw.edu.au/embryology/index.php?title=Main_Page

National Institute on Alcohol Abuse and Alcoholism:
http://www.niaaa.nih.gov/Pages/default.aspx

National Organization on Fetal Alcohol Syndrome:
www.nofas.org/default.aspx

Study Tools

Take advantage of additional online resources to help you study and ace your exams!

- Answers to case studies in the book
- Additional case studies and answers
- Interactive quiz bank with answer feedback
- Fully searchable e-book for quick lookup and studying on-the-go
- Expanded Media Menu with direct links to related Web sites and multimedia resources
- Supplemental readings

thePoint Online resources and links are available at http://thepoint.lww.com/DeLong2e.

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NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/ INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Fetal Alcohol Spectrum Defects (FAS, ARND, PFAS, ARBD)	Exposure to alcohol in utero	Alcohol crosses the placenta and is stored in amniotic fluid leading to prolonged exposure; exact mechanism is unknown.	Growth deficits, characteristic facial features and neurodevelopmental problems, cleft lip and/or palate is common	Not applicable	Surgical correction of congenital defects, behavioral therapy, medication to alleviate some behavioral symptoms such as those seen in attention deficit disorder	Discuss the potential problems associated with alcohol consumption during pregnancy with women of childbearing age, review medical histories of those with FASD for congenital heart defects and medications prior to treatment, discuss the potential for infective endocarditis in the presence of oral infection and the need for excellent homecare
TORCH Syndrome	Toxoplasmosis, rubella, cytomegalovirus, herpesvirus, and others	Most transmitted vertically through placenta, the exact mechanism of action is not known for most.	Premature birth, mental deficiency, hearing loss, vision impairment, congenital heart disease. Congenital syphilis causes Hutchinson incisors and mulberry molars.	Not applicable	Prevention is the key to eliminating this syndrome, vaccination, careful handling of potentially contaminated foods, avoiding contact with soil and cat litter. Congenital defects can be surgically corrected; Hutchinson incisors can be crowned.	Modify dental hygiene care based on the conditions present, discuss the potential for infective endocarditis in the presence of oral infection and the need for excellent homecare, refer pregnant women to CDC Web site for more information
Trisomy 21 (Down Syndrome)	Extra complete or partial chromosome #21 caused by nondisjunction, translocation, or mosaicism	Extra genetic material may cause overproduction of certain proteins that may lead to the disorder.	Short stature, poor muscle tone, simian crease, epicanthal fold, congenital heart defects common, increased risk of infections Midface hypoplasia, high narrow palate, anterior open bite and crowding, delayed eruption of primary and secondary dentition, high risk for early periodontal disease and loss of teeth	Not applicable	Surgical correction of congenital defects, lifetime follow-up care from a team of health care professionals Oral health care centers on correction of defects (clefts, malocclusion, etc.) and prevention of periodontal disease and other oral infections	Careful assessment of health history to identify congenital heart defects and other problems, discuss the potential for infective endocarditis in the presence of oral infection and the need for excellent homecare, instruct caregivers in homecare procedures if necessary, avoid excessive aerosol production during treatment
Klinefelter Syndrome	One or more extra X chromosomes in the male genotype caused most often by nondisjunction	Low testosterone and high levels of luteinizing and follicle-stimulating hormones cause the major problems, every additional X chromosome increases severity.	Tall, long arms and legs, lack of sexual development, infertility, gynecomastia, normal intelligence (more than one extra X may indicate mental deficiency), mitral valve prolapse Maxillary hypoplasia, taurodontism, and short roots	The presence of one Barr body for each additional X chromosome carried by the individual	Focuses on early hormone replacement, screening for osteopenia and osteoporosis and breast cancer, mastectomy for gynecomastia	A history of mitral valve prolapse indicates discussing the potential for infective endocarditis in the presence of oral infection and the need for excellent homecare.
Turner Syndrome	Monosomy of the X chromosome caused by paternal nondisjunction or mosaicism	Absence of estrogen is responsible for most abnormalities.	Short stature, low posterior hairline, webbing of the neck, congenital heart defects, hypertension, diabetes (II), hypothyroidism, average intelligence, learning disabilities High narrow palate, small mandible, malocclusion, secondary teeth erupt early, short roots, thin enamel	Not applicable	Focuses on growth hormone therapy and estrogen replacement therapy properly timed to optimize growth potential, surgical correction of cardiac defects, medications for hypertension, diabetes, etc.	Review medical history carefully for indications of cardiac defects, hypertension and endocrine disorders, modify treatment as indicated, discuss potential for infective endocarditis in the presence of oral infection and the need for excellent homecare, refer for early orthodontic evaluation observe young patients for characteristics of disorder and refer for evaluation

Chapter 6 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/INTRAORAL)	MICROSCOPIC/RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Marfan Syndrome	Autosomal dominant genetic disorder (chromosome 15, FNB1 gene)	Decreased production of fibrillin causes abnormally flexible connective tissues leading to the symptoms of this disorder.	Very tall, long arms, legs, fingers and toes, breast bone and spinal deformities, joint laxness, ocular defects, cardiovascular defects (valve defects, aneurysms) High narrow palate, malocclusion, TMJ dysfunction, bifid uvula	Not applicable	Anticipate and correct skeletal and ocular problems, evaluate for cardiac abnormalities and closely monitor over lifetime, medicate to prevent cardiovascular problems and correct with surgery when necessary	Review medical history carefully for cardiovascular problems, modify treatment as necessary, use prophylactic antibiotic medication when indicated, discuss the potential for infective endocarditis in presence of oral infection and need for excellent homecare, identify bifid uvula as a possible indication of LDS, refer patients for evaluation
Cleidocranial Dysplasia	Autosomal dominant genetic disorder (chromosome 6, deletion CBFA1 gene)	CGFA1 gene controls creation of osteoblasts	Short stature, hypoplastic or missing clavicles, frontal bossing, wide nasal root, depressed bridge, multiple supernumerary teeth, delayed exfoliation of primary and eruption of secondary teeth, clefts are common	Not applicable	Skeletal abnormalities do not usually require treatment unless scoliosis is identified.	Numerous dental abnormalities caused by aberrant eruption and exfoliation patterns and supernumerary teeth indicate early preventive care and orthodontic intervention.
Treacher Collins Syndrome	Autosomal dominant genetic disorder (chromosome 5, TCOF1 gene mutation)	Unknown	Eyes slant down, lower lid notched, missing most eyelashes, hypoplastic zygoma, maxilla and mandible, malformed or missing ears, some degree of hearing loss High vault, clefts are common, severe malocclusion, open bite, wide proximal spaces, displaced teeth	Not applicable	Surgical correction of facial defects, orthodontics, hearing aids or cochlear implants	Early preventive care and orthodontic intervention is essential; regular dental care should continue throughout life.
Ehlers-Danlos Syndrome	Autosomal dominant inheritance is most common.	Production of abnormal collagen leads to weakness in structures composed of collagen.	Excessively loose joints dislocate easily; hyperelastic, thin, loose skin; fragile skin, mucous membranes, blood vessels and other tissues; defective heart valves common; degenerative bone and joint conditions TMJ dysfunction; Gorlin sign; fragile, easily traumatized oral mucosa; malformed crowns and roots; abnormal enamel and dentin	Not applicable	Treatment focuses on preventing damage to joints and stabilizing them; monitoring individual for development of aneurysms, heart valve defects, and signs of organ rupture.	Careful assessment of health history to identify heart defects and discuss the potential for infective endocarditis in the presence of oral infection and the need for excellent homecare. Treatment modifications for fragile membranes, poor wound healing, and hypermobility of TM joint; avoid trauma; protect sutures with splints or dressings
Papillon-Lefèvre Syndrome	Autosomal recessive inheritance (chromosome 11, Cathepsin C gene defect)	Theory points to defective chemotactic and phagocytic functions in neutrophils, T-lymphocyte defect, or decreased numbers of NK cells	Scaly red hyperkeratosis on palms and soles; hyperhidrosis, body odor; increased chronic and recurrent infections Progressively severe gingival inflammation after eruption of first tooth, severe periodontal attachment loss; resolves when teeth are lost and recurs with eruption of the first permanent tooth, most teeth lost by age 15	Significantly decreased WBC count, neutrophils, and NK cells	Topical retinoids and mechanical exfoliation of hyperkeratotic areas; frequent preventive care and excellent homecare for periodontal infections; extraction of hopeless teeth	Frequent preventive appointments and homecare instructions focused on diligence and effectiveness
Gingival Fibromatosis	Autosomal dominant and recessive, also associated with different syndromes	Slowly progressive overgrowth of the fibrous tissues of the gingiva occurring after eruption of the first tooth	Generalized or localized, maxillary arch more often than mandible, may cause failure or delayed eruption of teeth; localized form affects maxillary posterior area most often; growth continues until crowns of teeth are covered; stops when edentulous.	Dense collagenous tissue with long thin rete ridges deep into connective tissue	Repeated surgical removal of excess tissues; surgical exposure of erupting teeth	Rule out syndromes associated with hyperplasia and other causes of hyperplasia such as medications Excellent homecare techniques and frequent preventive appointments to minimize additional hyperplasia due to inflammation

continues

Chapter 6 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/INTRAORAL)	MICROSCOPIC/RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
X-linked Hyperhidrotic Ectodermal Dysplasia (EDA)	X-linked recessive (mutation of ED1 gene)	Abnormal development of tissues derived from embryonic ectodermal cells	Little or no hair, defective hair follicles; few or no sweat glands, tendency for hyperthermia; skin is thin, smooth, and dry. Frontal bossing, midface/maxillary hypoplasia. Anodontia or hypodontia, delayed eruption; malformed teeth; xerostomia.	Not applicable	Treatment focuses on alleviating the symptoms and preventing overheating especially during infancy and childhood.	Severe xerostomia causes increased biofilm and caries risk, makes use of removable appliances difficult; multiple restorations and xerostomia increase homecare difficulty; develop user-friendly homecare regimens periodic fluoride varnish treatments essential.
Cleft Lip/Palate	Multifactorial interaction of genetic and environmental factors	Incomplete or no fusion of the palate, premaxilla, and soft tissues during weeks 6–8 in utero	Clefts may affect the lip, palate, or submucosal structures of the soft palate; they may be unilateral or bilateral.	Not applicable	Treatment focuses on repairing the clefts and restoring function; later treatment repairs dental abnormalities with surgery and/or orthodontics and restorations.	Patient education about helping to prevent clefts with adequate levels of folic acid during childbearing ages

CHAPTER 7

Endocrine Disorders

KEY TERMS

Acidosis	Hypoglycemic unawareness
Acanthosis nigricans	Hypophysis
Acromegaly	Adenohypophysis
Adenohypophysis	Neurohypophysis
Advanced glycation end products	Macroglossia
Autoimmune thyroiditis/Hashimoto thyroiditis	Macrovascular
Basal metabolic rate	Microangiopathy
Dental erosion	Myxedema
Diabetes mellitus	Negative feedback system
Diabetic dermopathy	Nephropathy
Diabetic ketoacidosis	Neurohypophysis
Estimated average glucose (eAG)	Neuropathy
Exophthalmos	Autonomic neuropathy
Fasting plasma glucose test	Peripheral neuropathy
Follicles	Oral glucose tolerance test
Gestational diabetes mellitus	Osteopenia
Gigantism/giantism	Parafollicular cells
Glycosylation	Polydipsia
Goiter	Polyphagia
Graves disease	Polyuria
Hemoglobin A1c (HbA1c)	Prayer sign
Hormone	Prediabetes
Hypercalcemia	Pseudoanodontia
Hyperglycemia	Retinopathy
Hyperosmolar hyperglycemic state	Striae
Hyperinsulinism	Target cell
Hyperreflexia	Tetany
Hypoglycemia	Thyroid storm

LEARNING OUTCOMES

1. Define and use the key terms listed in this chapter.
2. Briefly describe the functioning of the endocrine system.
3. Discuss the function of each organ and name the hormones involved.
4. State the etiology, method of transmission, and pathogenesis of the disorders discussed in this chapter.
5. Describe the extraoral, perioral, and intraoral characteristics of the disorders discussed in this chapter.
6. Note the dental implications and potential dental treatment modifications associated with the disorders discussed in this chapter.
7. Describe the differences between the clinical characteristics of hypothyroidism and hyperthyroidism.
8. Discuss the conditions that can lead to the formation of a goiter.
9. Describe the important epidemiologic factors associated with diabetes mellitus.
10. Describe the hemoglobin A1C test, how it is used, and the significance of the results.
11. Differentiate between hypoglycemia, diabetic ketoacidosis (DKA), and hyperosmolar hyperglycemic state as they relate to diabetes.
12. Discuss the chronic complications associated with diabetes mellitus.
13. Describe how the defective host response in diabetes mellitus can lead to periodontal destruction.
14. Identify the two endocrine abnormalities that increase the risk of acquiring an oral fungal infection.
15. Describe the differences and similarities between diabetes insipidus and diabetes mellitus.

CHAPTER OUTLINE

The Endocrine System
Organs and Hormones of the Endocrine System
General Function of the Endocrine System
Endocrine System Disorders
Hypothalamus and Pituitary Gland
Diabetes Insipidus
Hypopituitarism
Hypersecretion of Growth Hormone
Thyroid Gland
Hypothyroidism
Hyperthyroidism
Parathyroid Gland
Hypoparathyroidism
Hyperparathyroidism
Adrenal Gland
Adrenocortical insufficiency
Acute Adrenal Insufficiency or Adrenal Crisis
Hyperadrenalism
Pancreas
Diabetes mellitus type 1
Diabetes mellitus type 2
Prediabetes
Gestational Diabetes Mellitus

RELATED CLINICAL PROTOCOLS

#4 Treating Patients with Xerostomia
#16 Oral Health Care Management for the Patient with Diabetes

The Endocrine System

There are two major communication systems within the body, the endocrine system and the nervous system. Both systems are essential to the correct functioning of the body, and each system depends on the other. The nervous system is responsible for fast processes or immediate actions such as movement, thought, breathing, and heartbeat, while the endocrine system is responsible for the slower processes such as growth, metabolism, maintaining electrolyte balance, and the immune response. Both systems use chemical messengers to relay information to and from body organs, tissues, and cells.

Organs and Hormones of the Endocrine System

Two types of glands are found in the body, exocrine and endocrine. Exocrine glands secrete their products onto the surface of skin or mucous membranes by means of a system of ducts. For example, the parotid gland secretes saliva through the parotid duct into the mouth. The endocrine system is composed of glands that secrete their products or chemical messengers directly into the circulatory or lymphatic systems or into local tissues without the use of ducts. The products they secrete are called **hormones.** Hormones regulate the functions of organs and systems in the body. Most hormones affect more than one type of cell or tissue and have different effects on each type of tissue. Some hormones can only function when there are several of them working together to create an effect. Specific hormones will only react with cells that have receptors for that hormone on their cell membranes. Cells having these receptors are called the **target cells** for that hormone. An entire organ such as the thyroid gland or a specific tissue such as fat tissue will contain cells all having receptors for one or more specific hormones, thereby creating a target organ or tissue. The hormone stimulates the target cell to do something or to stop doing something, depending on the type of hormone. When the action is complete, the hormone will stop being released until the body is signaled by another substance, possibly another hormone, to start the action again. The major endocrine glands and their locations are illustrated in Figure 7.1. To understand the disorders associated

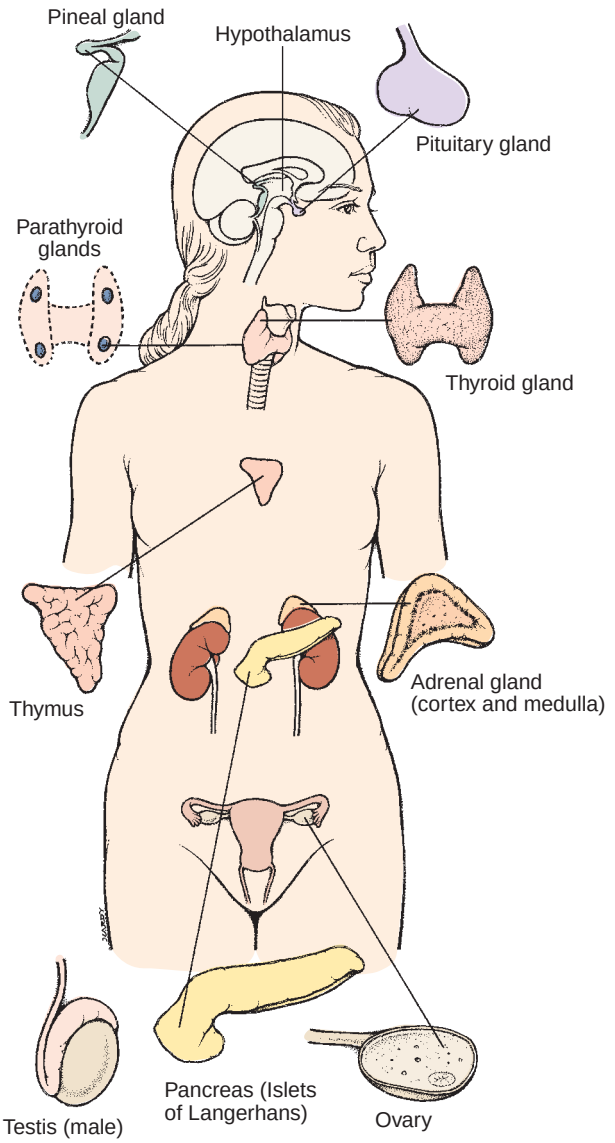

FIGURE 7.1. Endocrine glands. Illustration depicting the location of the endocrine glands. (From Stedman's medical dictionary. 27th ed. Baltimore: Lippincott Williams & Wilkins, 2000.)

TABLE 7.1 **Hypothalamic Hormones**

Hormone	Target	Function
Thyrotropin-releasing hormone (TRH)	Anterior pituitary	Stimulates the pituitary to release thyrotropin
Gonadotropin-releasing hormone (GnRH)	Anterior pituitary	Follicle-stimulating, luteinizing
Growth hormone–releasing hormone	Anterior pituitary	Stimulates growth hormone release
Adrenocorticotropin-releasing hormone	Anterior pituitary	Stimulates the release of adrenocorticotropin
Prolactin-releasing hormone	Anterior pituitary	Stimulates the release of prolactin
Oxytocin	Posterior pituitary	Stimulates labor
Antidiuretic hormone (ADH) (vasopressin)	Posterior pituitary	Stimulates the kidney to reabsorb water

with the endocrine system, one must understand how the system functions correctly. The following is a brief review of the processes involved in the proper functioning of the endocrine system.

General Function of the Endocrine System

Endocrine functioning begins with the hypothalamus, a gland located superior to the pituitary gland in the area of the midbrain. The hypothalamus serves as the central receiving area for input from the nervous system regarding changes in the environment, such as temperature, or changes in the body, such as pain or feelings of fright or terror. The hypothalamus then relays this information using the hormones listed in Table 7.1 to the next gland in the hierarchy, the pituitary gland or **hypophysis.** The pituitary gland is located directly beneath the hypothalamus in the sella turcica and is connected to the hypothalamus by the pituitary stalk (Fig. 7.2). The pituitary is made up of an anterior portion, or **adenohypophysis,** and a posterior portion, or **neurohypophysis**. The anterior pituitary receives releasing hormones from the hypothalamus by way of the connecting blood flow (Table 7.1). Using thyrotropin-releasing hormone (TRH) as an example, the pituitary gland secretes thyroid-stimulating hormone (TSH), which travels to the thyroid gland, the target organ in this case. The TSH stimulates the cells of the thyroid gland to create thyroid hormones such as thyroxine, which, in turn, is secreted by the thyroid gland to travel to cells that have a receptor for thyroxine. Thyroxine stimulates each cell, depending on the type, to start performing or to increase or decrease performance of a specific function. Table 7.2 lists the pituitary hormones, their target glands or tissues, and their functions. Table 7.3 lists endocrine hormones, their

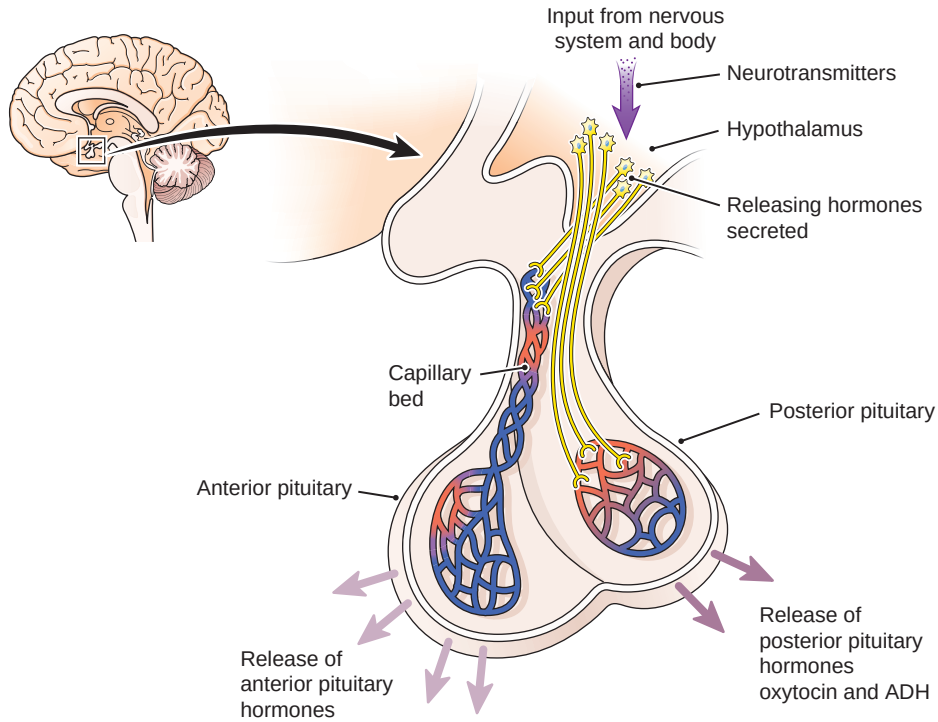

FIGURE 7.2. Hypothalamus and the pituitary gland. This illustration shows the intimate relationship between the hypothalamus and the pituitary gland.

TABLE 7.2 **Pituitary Hormones**

Hormone	Target Cells or Tissues	Function
Growth hormone (GH)	Bones, muscles, and other tissues	Increases protein synthesis and growth
Adrenocorticotropic hormone (ACTH)	Adrenal cortex	Stimulates the production and release of hormones from the adrenal cortex
Thyroid-stimulating hormone (TSH)	Thyroid gland	Stimulates the production and release of thyroxine
Follicle-stimulating hormone (FSH)	Gonads	Stimulates the growth and maturation of the egg and sperm
Luteinizing hormone (LH)	Gonads	Stimulates the release of sex hormones from the ovaries and testes
Prolactin	Mammary glands	Stimulates milk production
Oxytocin	Uterus and breasts	Initiates labor and milk flow
Antidiuretic hormone (ADH)	Kidneys	Increases water retention and raises blood pressure
Endorphins	Neurons in the spinal cord and brain	Decreases pain sensations

functions, target cells, and the endocrine gland by which they are secreted.

The posterior pituitary receives hormones produced by the neurons of the hypothalamus. These hormones travel along the nerve fibers from the hypothalamus to the posterior pituitary, where they are stored until needed. The hormones secreted by the posterior pituitary are not releasing hormones (see Table 7.1); they do not stimulate another gland to secrete another hormone; instead, they act directly on the target cells designed to provide the desired function.

TABLE 7.3 **Select Endocrine Hormones and Their Functions**

Hormone	Secreting Tissue or Gland	Target Cells or Tissues	Function(s)
Thyroxine, triiodothyronine	Thyroid	Almost all	Maintains metabolism, is crucial in growth of the brain and CNS
Calcitonin	Thyroid	Bones	Stimulates bone formation, regulates the amount of calcium in the blood
Parathormone	Parathyroids	Bones	Resorbs bone, regulates blood calcium levels
Thymosins	Thymus	Immune system cells	Activate T cells in the lymphatic system
Insulin	Pancreas	Muscles, fat, liver, others	Stimulates the uptake and use of glucose, increases the creation of glycogen and fat from glucose
Glucagon	Pancreas	Liver	Increases blood sugar by increasing the metabolism of glycogen
Somatostatin	Pancreas	Digestive system and cells of the pancreas	Inhibits the release of insulin and glucagon, decreases all actions of the digestive tract
Epinephrine	Adrenal medulla	Heart, blood vessels	Increases heart rate, increases blood flow to muscles, increases glucose level in the blood, initiates the fight or flight response (sympathetic nervous system)
Norepinephrine	Adrenal medulla	Heart, blood vessels	Regulates the normal actions of the heart, blood vessels, etc. (sympathetic nervous system)
Glucocorticoids	Adrenal cortex	Immune system, many others	Anti-inflammatory action, affect metabolism of nutrients, maintain blood glucose levels, modify the effects of stress, involved in growth
Mineralocorticoids (aldosterone)	Adrenal cortex	Kidney	Stimulate excretion of potassium and reabsorption of sodium from the urine
Gastrin	Stomach lining	Stomach	Stimulates release of digestive juices and stomach muscle contractions
Melatonin	Pineal gland	Hypothalamus	Regulates day and night cycles and other biorhythms
Estrogens	Ovaries	Female reproductive organs and other tissues	Promotes female characteristics and sexual behavior
Progesterone	Ovaries	Uterus	Supports pregnancy, maintains female sexual characteristics
Androgens (testosterone)	Testes	Male reproductive organs and other tissues	Promotes male sexual characteristics and behavior, sperm production

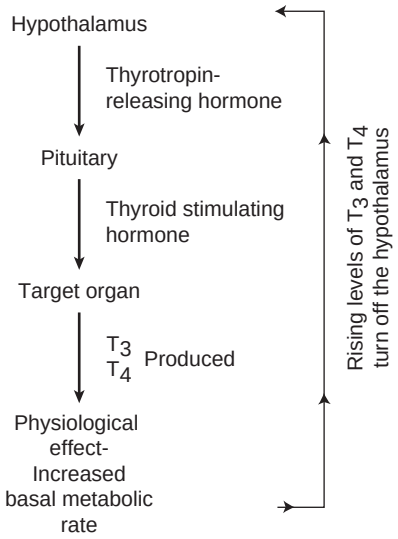

FIGURE 7.3. Negative feedback system. Illustration of how the negative feedback system functions, using the thyroid gland as an example.

For example, the hypothalamus receives a signal that it is time for a pregnant woman's labor to begin. In response to the stimulus, the hypothalamus triggers the posterior pituitary to release oxytocin that is picked up by the circulatory system and received by receptors on the muscle cells of the uterus, which start to contract and begin labor.

The endocrine system is regulated in most cases by a **negative feedback system**. The negative feedback system works like a thermostat in your home (i.e., when the temperature drops below a set level, the thermostat recognizes it and starts the furnace). When the temperature gets to, or slightly above, the set temperature, the thermostat senses this and shuts off the furnace. Thus, when the hypothalamus notices a drop in a particular hormone, it sends a message to the pituitary gland to secrete the tropic or releasing hormone. The releasing hormone is received by the target cells in a specific glandular tissue, which stimulates the gland to produce the needed hormone, increasing the level of that hormone. When the level is appropriate, the hypothalamus stops sending out the tropic hormone, and the target cells will not be stimulated to produce the hormone until the level drops again (Fig. 7.3). While the production of most hormones is regulated with a negative feedback system, there are a few examples of positive feedback regulation, occurring mainly in the female reproductive system. In positive feedback regulation, an increasing level of one hormone stimulates the release or increased production of a second hormone. The process is terminated when the original hormone level drops, thereby causing the production of the second hormone to decrease or stop. A properly functioning endocrine system is essential to the well-being of each person. When the system malfunctions, life-threatening disorders occur.

Endocrine System Disorders

Endocrine disorders can result from numerous abnormalities. The pituitary gland may fail to secrete the appropriate tropic or releasing hormone, or it may not receive the appropriate commands from the hypothalamus. The hormone produced could be defective because there is not enough of a crucial ingredient or the genetic code for that protein could be defective or the secretory system could be damaged. The blood or lymphatic system may fail to transport the hormone to the target organ, or the hormone could be inactivated by a substance or drug in the blood or lymphatic system. There could also be a problem with the receptor or target cells that could be blocked from receiving the hormone or missing altogether. Growths or tumors can form within the glands and interfere with production or release of the hormones or cause unregulated production and secretion of too much of a hormone. Finally, neoplastic growths can become so anaplastic that even if the tissue of origin is not a glandular tissue, the neoplastic cells can start producing their own hormones. Whatever the cause, the symptoms are usually the result of either too little or too much of a hormone, and thus the names of the disorders reflect either hypofunction or hyperfunction of the hormone or gland, for example, hyperthyroidism. The following sections discuss information specific to the functioning of each gland and examples of disorders related to them.

Hypothalamus and Pituitary Gland

As previously explained, these two glands work in conjunction to oversee the entire endocrine system. Problems associated with the hypothalamus will manifest as pituitary dysfunction because the role of the hypothalamus is to signal the pituitary to release its hormones. See Tables 7.1 and 7.2 for a listing of the hormones secreted by these glands and their targets and functions. The following conditions are examples of hypothalamic or pituitary disorders.

Diabetes Insipidus

A lower-than-normal level of antidiuretic hormone (ADH), also called vasopressin, causes a disorder known as diabetes insipidus. This is not to be confused with diabetes mellitus, which results from an insulin deficiency or dysfunction. The blood glucose level of an individual with diabetes insipidus should be normal. ADH controls the reabsorption of water into the body by the kidneys. An inadequate level of ADH causes large amounts of urine to be produced, which quickly leads to dehydration and electrolyte imbalances. Diabetes insipidus can be caused by tumors of the hypothalamus or pituitary, head trauma, brain aneurysms, or infections. It can also occur when target cells in the kidneys do not respond to ADH because of an acquired or genetic kidney disorder. This is a rare disorder that affects males and females equally and can be found in all ages and races. Affected individuals have intense thirst, or **polydipsia,** and excessive urination, or **polyuria.** This disorder is called diabetes insipidus because it shares these two universal symptoms with diabetes mellitus. If water intake is inadequate, dehydration will occur rapidly and can be life threatening. The treatment for diabetes insipidus is administration of desmopressin, a synthetic analogue (substance that functions in a similar fashion) of

ADH, maintenance of an adequate water intake, and a low-sodium diet. The prognosis for these individuals is excellent as long as they maintain an adequate water intake.

There has been no evidence of increased dental disease in these patients. However, dehydration is associated with xerostomia, and those who are at risk for xerostomia should have their salivary flow assessed. If insufficient saliva is found, treatment protocols for xerostomia should be followed (see Clinical Protocol #4).

Hypopituitarism

Hypopituitarism is a general name given to a deficiency of any of the pituitary hormones. The specific cause of the deficiencies may be related to the hypothalamus or the pituitary gland. Most of these cases are caused by pituitary neoplasms. Approximately 70 to 90% of the gland must be destroyed for deficiencies to become obvious (Porth, 2011). Hypopituitarism results in the underproduction of a tropic or release-stimulating hormone that in turn results in a lower level of the target hormone such as growth hormone or thyroid hormone. The characteristics of hypopituitarism are determined by the hormones affected. For example, if TSH is affected, you would expect to see symptoms of hypothyroidism; adrenocorticotropic hormone (ACTH) would cause hypoadrenalism, etc. The age of the individual will also determine the extent and severity of the symptoms. Children need these hormones to develop normally; therefore, a deficiency in any of these causes more severe problems in the young than in the adult.

In adults, chronic deficiency of pituitary hormones causes a type of premature aging. The skin becomes thin, pale, dry, and wrinkled and there is little or no sweating. Axial and pubic hair is lost, and the remaining hair becomes soft and fine. Secondary sexual characteristics become less apparent, and sexual libido is lost. Blood pressure and metabolism are low, and the individual tends to be cold intolerant, lethargic, and weak. Life-threatening adrenal crisis can occur if the adrenal glands do not produce enough cortisol (discussed later in the chapter). Infants will present with failure to thrive and growth retardation. If the thyroid gland is not functioning, congenital hypothyroidism will cause mental deficiency. Older children will not start puberty, and secondary sexual characteristics will not develop. Major hormone deficiencies are usually diagnosed at an early age because of the lack of growth or failure to thrive consistent with this type of disorder. Children will tend to have delayed eruption of the primary and permanent teeth, with associated delayed exfoliation of the primary dentition. The abnormal eruption/exfoliation pattern may cause significant malocclusion. The clinician should be prepared to educate patients and families about this possibility and manage the malocclusion, if any.

Treatment depends on the specific cause and deficiencies involved. Pituitary tumors should be removed if possible. A deficiency in growth hormone would warrant consideration of hormone therapy designed to optimize growth, etc. Untreated adrenal insufficiency is associated with a high risk of premature death. In addition, recent evidence appears to demonstrate an increase in premature adult cardiac deaths in individuals who discontinued the use of supplemental growth hormone after reaching their full linear growth potential (height) at puberty (Hoffman, 2009).

Hypersecretion of Growth Hormone

Hypersecretion of growth hormone by the anterior pituitary affects patients differently, depending on the individual's age. **Gigantism** or giantism is the result of hypersecretion of growth hormone prior to the end of puberty and manifests as excessive growth in the skeletal system, producing very tall individuals (Fig. 7.4). Hypersecretion of growth hormone after puberty causes **acromegaly**, which manifests with the enlargement of soft tissues and bones of the hands, feet, face, and skull (Fig. 7.5). In addition, internal organs can become enlarged, and nerves can become entrapped and pinched in narrowing foramina. Excess soft tissue may cause sleep apnea, respiratory obstructions, and an increased risk for respiratory infections.

Acromegaly causes lengthening of the face, frontal bossing, enlargement of both the maxilla and mandible,

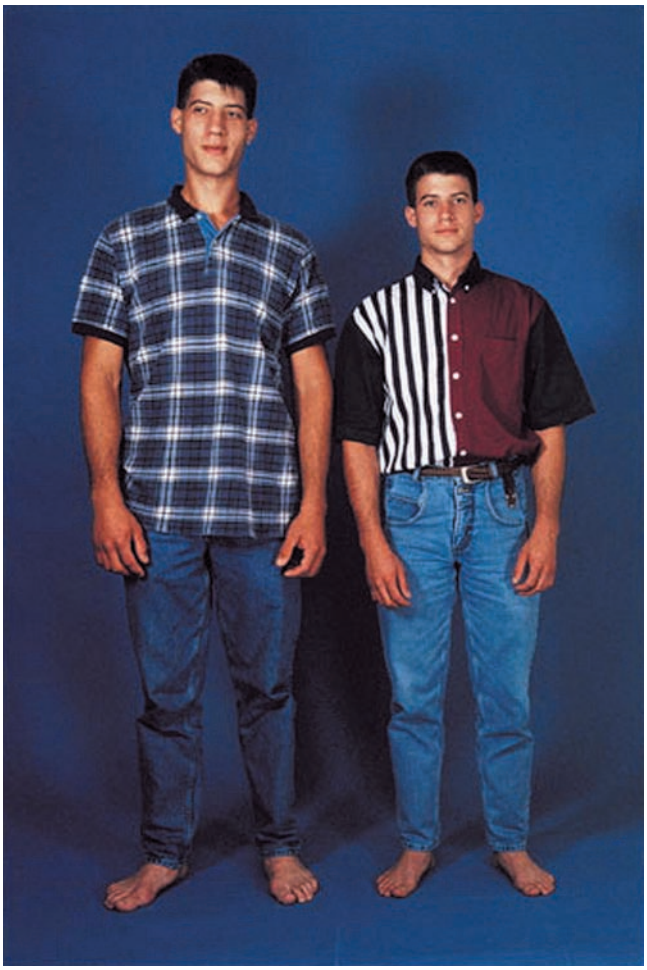

FIGURE 7.4. Giantism. A 22-year-old man with giantism due to excessive growth hormone is shown to the left of his identical twin. (From Gagel RF, McCutcheon IE. Images in clinical medicine. N Engl J Med 1999;340:524.)

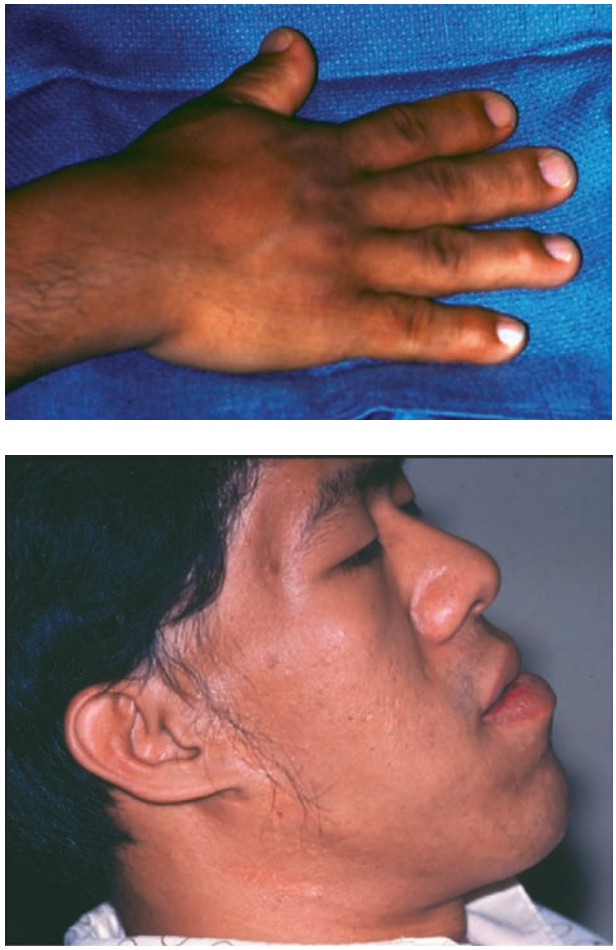

FIGURE 7.5. Acromegaly. Enlarged hands (**A**) and facial features (**B**) in a patient with acromegaly. (Courtesy of Dr. Géza Terézhalmy.)

class III occlusion, and widely separated teeth (Fig. 7.6). The tongue enlarges (**macroglossia**), and the dorsal surface may become deeply fissured. Dental treatment can be complicated by the severe malocclusion caused by excessive growth of the jaw bones. Removable prosthetic appliances may be difficult for the patient to tolerate because of macroglossia. Medical treatment focuses on removing the cause, usually a pituitary tumor, if possible.

FIGURE 7.6.. Acromegaly. Enlargement of the mandible with interproximal spacing and characteristic class III occlusion. (Courtesy of Dr. Géza Terézhalmy.)

Thyroid Gland

The thyroid gland develops in the area of the base of the tongue at the foramen cecum. During normal development, it migrates into the neck along the thyroglossal duct tract. Infrequently, the gland does not migrate and remains at the base of the tongue as a lingual thyroid (Fig. 7.7).

The thyroid gland consists of **follicles,** or microscopic sacs, containing a protein called *colloid.* The cells that make up the walls of these sacs are called follicular cells and produce two types of thyroid hormone, *triiodothyronine* (T_3) and *thyroxine* (T_4). In addition, **parafollicular** or C cells produce calcitonin, which inhibits the release of calcium from bones into the blood and other fluids. The functions of the thyroid hormones are listed in Box 7.1.

Disorders of the thyroid gland normally manifest symptoms associated with either an excess or deficiency of thyroid hormones. One physical manifestation of thyroid disease is a **goiter** or enlarged thyroid gland caused by hypertrophic or hyperplastic growth. If the thyroid gland is not producing enough thyroid hormone or the hormone is defective, the pituitary will continue to release TSH to increase the gland's production of thyroid hormones causing chronic enlargement of the thyroid gland as it attempts to produce enough thyroid hormone to "turn off" the release of TSH by the pituitary. Since the cells that produce the thyroid hormones, T_3 and T_4, are

FIGURE 7.7. Lingual thyroid. Failure of the thyroid to descend to its proper place in the neck may result in a "lingual" thyroid. Since this may be the only thyroid tissue an individual possesses, surgical removal should be only undertaken when the thyroid status of the individual is investigated thoroughly. ("Ectopic thyroid–lingual 01," (c) 2011 Bipul Kumar Choudhury et al., used under a Creative Commons Attribution-ShareAlike license: *http://creativecommons.org/licenses/by/2.0/*, accessed February 5, 2012.)

BOX 7.1 Thyroid Hormone Functions

Hormone	Function
Thyroxine and triiodothyronine	■ Regulates BMR[a] and body temperature ■ Regulates lipid metabolism ■ Regulates carbohydrate metabolism ■ Affects all aspects of linear growth ■ Crucial in the development of the brain before and after birth ■ Regulates heart rate, contractibility, and output ■ Regulates vasodilation ■ Regulates respiratory rate ■ Regulates gastrointestinal activity ■ Affects libido and fertility
Calcitonin	■ Decreases blood calcium levels by inhibiting resorption of bone by osteoclasts and reabsorption of calcium and phosphorus in the kidneys

[a]The basal metabolic rate is defined as the amount of oxygen consumed by the body (cells) while at rest (not physically active).

incapable of increased hormone production, they must adapt to the increased demand by becoming hyperplastic or hypertrophic. A goiter can also be observed when there is excessive production of thyroid hormones by the thyroid gland. In this instance, the gland is not "turned off" even though there is an abundance of thyroid hormones circulating through the body. Neoplasms of the thyroid gland, benign or malignant, will cause an enlarging thyroid gland. However, these enlargements are not considered goiters because they are not responding to hormone stimulation. Goiters or other thyroid gland enlargements may be observed by the dental professional during the head and neck examination. The goiter may be large or it may present as a subtle diffuse swelling of the neck just inferior to the thyroid cartilage (Fig. 7.8). The patient should be referred to a physician for evaluation if the presence of an enlarged thyroid gland is suspected. Thyroid disorders that cause hypofunction or hyperfunction of the gland are common.

NAME: Hypothyroidism

Etiology: Internationally, the most common cause of hypothyroidism is an iodine-deficient diet. Without iodine, the thyroid hormone that is produced is defective and nonfunctional. In the United States, the most common cause of hypothyroidism is **autoimmune thyroiditis,** also known as **Hashimoto thyroiditis.** In this case, the body sees the thyroid tissue as an antigen, and a chronic immune reaction occurs resulting in progressive destruction of the thyroid tissues and a gradual decrease in thyroid hormones. Congenital hypothyroidism is seen in infants and can result from a defect in the genes determining how the gland synthesizes the hormones, resulting in defective hormones or thyroid agenesis.

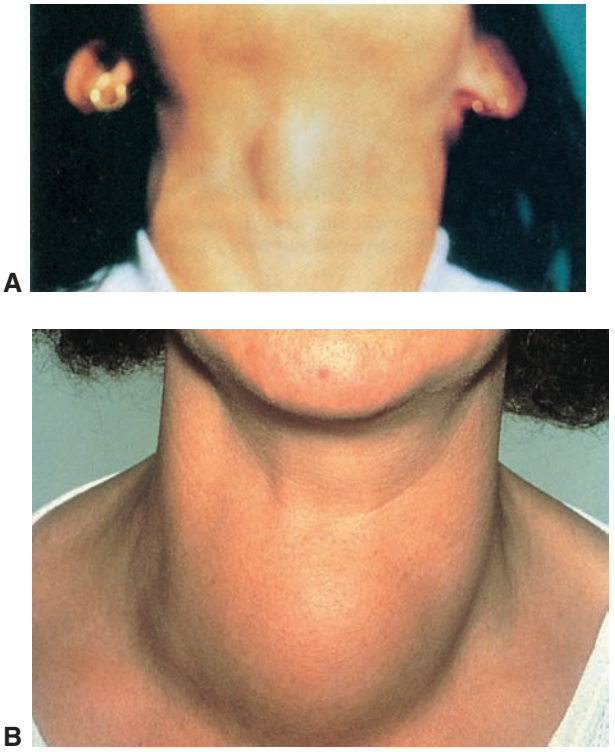

FIGURE 7.8. Goiter. **A.** Small goiter. (From Moore KL, Dalley AF II. Clinical oriented anatomy. 4th ed. Baltimore: Lippincott Williams & Wilkins, 1999.) **B.** Large goiter. (From Weber J, Kelley J. Health assessment in nursing. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

Method of Transmission: Genetic transmission of hypothyroidism usually follows an autosomal recessive inheritance pattern. Other forms of hypothyroidism are not transmitted; rather, they occur as unrelated events.

Epidemiology: Hypothyroidism occurs in approximately 3.7% of the United States population. It is most common in whites and least common in blacks. It is two to eight times more likely that a woman will have hypothyroidism than a man, and the risk of having hypothyroidism increases with age (Bharaktiya et al., 2011). Hashimoto thyroiditis is the most common cause of this disorder after the age of 6 (Lee et al., 2011). Congenital non–iodine-deficient hypothyroidism occurs in about 1 of every 4,000 live births (Postellon & Daniel, 2011).

Pathogenesis: Decreased synthesis and release of hormones produced by the thyroid or the production of defective hormones leads to the characteristic clinical manifestations described in the sections below.

Extraoral Characteristics: The general physical characteristics of hypothyroidism are listed in Table 7.4. Individuals with congenital hypothyroidism exhibit similar symptoms in addition to generalized severe growth retardation, lack of muscle development, and mental deficiency. Figure 7.9A shows the edematous facial features evident in adults with hypothyroidism. Figure 7.9B shows the same individual after treatment. This type of edema

TABLE 7.4 **Clinical Manifestations of Hypothyroidism**

System	Manifestation
Nervous	Lethargy, memory loss, slowed thinking, depression, hearing loss, night blindness, cold intolerance, and mental agitation
Integumentary	Edema of the face, hands, and feet; skin is dry, rough, pale, and cool to the touch; hypohidrosis; bruises easily and heals slowly; hair is dry and brittle.
Cardiovascular	Decreased heart rate and output, edema, atherosclerosis, enlarged heart with dilated chambers
Gastrointestinal	Decreased peristalsis leads to constipation and atrophy of the muscles of the system; anorexia, weight gain.
Reproductive	Women: irregular, heavy menstruation; progesterone deficiency; and decreased libido Men: decreased libido, erectile dysfunction, and low sperm count
Musculoskeletal	Generalized muscle weakness, slowed reflexes, decreased bone formation and resorption and increased bone density, joint pain and stiffness
Pulmonary	Decreased respiratory rate and dyspnea
Blood	Anemia due to inadequate absorption of iron, folate, and/or vitamin B_{12} in the intestinal tract; increased cholesterol levels
Renal	Increased water retention

(**myxedema**) is caused by the accumulation of a substance within connective tissue cells that causes water retention, which can lead to malfunction of organs such as the heart and digestive tract.

Perioral and Oral Characteristics: In addition to generalized facial edema, puffy lips, enlarged gingival tissues (Fig. 7.10), and macroglossia are often present. Pharyngeal edema may result in a coarse, raspy voice and dysphagia. Delayed exfoliation of the primary teeth and delayed eruption of both the primary and the permanent teeth are also expected.

Distinguishing Characteristics: Reports of symptoms associated with hypothyroidism and clinical observation of the characteristic goiter or neck swelling and facial edema warrant a referral for a physical evaluation.

Significant Microscopic Features: Not applicable

Dental Implications: The etiology of gingival edema should be investigated, and if no identifiable cause can be found, the patient should be referred for a medical evaluation, especially if other symptoms are present. Delayed eruption may produce **pseudoanodontia** (the temporary absence of teeth), which may have to be managed with prosthetics, depending on the severity and duration of symptoms.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment focuses on removing the cause if possible and replacing deficient hormones with oral supplements. Normal function will be achieved shortly after starting the supplemental hormones. Treated individuals can expect a normal life. Untreated hypothyroidism has a poor prognosis and a high mortality rate (Lee et al., 2011). Congenital hypothyroidism results in irreversible damage because thyroid hormones are essential for the proper development of the fetus. If replacement therapy is started at birth, the damage can be minimized, but there may be lingering developmental problems. Neonatal

FIGURE 7.9. Hypothyroidism. **A.** Before treatment: Facial features showing generalized edema. **B.** After treatment: Edema has resolved and normal facial features have been restored. (From CDC/Dr. J. Lieberman; Dr. Freideen Farzin, University of Tehran. Available at: *http://phil.cdc.gov/phil/home.asp ID#12564 and ID#12568*.)

FIGURE 7.10. Hypothyroidism. Enlarged gingiva associated with edema from hypothyroidism. (From CDC/Dr. J. Lieberman; Dr. Freideen Farzin, University of Tehran. Available at: *http://phil.cdc.gov/phil/home.asp ID#12565*.)

screening programs in the United States have all but eradicated the effects of this disorder in infants.

NAME: Hyperthyroidism

Etiology: The most common cause of hyperthyroidism is an autoimmune reaction caused by autoimmune antibodies that bind to TSH hormone receptors and induce the thyroid to create more thyroid hormone. The thyroid enlarges, or becomes hypertrophic, to compensate for this added requirement (Lee & Ananthakrishnan, 2011). This disorder is called **Graves disease**. Hyperthyroidism can also be caused by an infectious process, a benign hyperfunctioning tumor, or transformation of a nontoxic goiter (one that is not secreting too much thyroid hormone) to a toxic goiter (one that is hyperactive). Hyperthyroidism, no matter what the cause, presents with similar clinical manifestations. The focus here is on Graves disease, since it is the most common form of hyperthyroidism in the United States.

Method of Transmission: Inheritance appears to have the strongest influence on the development of Graves disease. More than one gene has been identified as influencing the development of Graves disease and multifactorial inheritance is suspected because the rate of hyperthyroidism between identical twins is only about 30 to 50%. The exact environmental causes are unknown, but smoking has been associated with an increased risk of developing this disorder (Rubin et al., 2012; OMIM %275000, 2011).

Epidemiology: In the United States, cases of hyperthyroidism occur in about 1 of every 2,000 people. Graves disease is 7 to 10 times more common in women than in men (Rubin et al., 2012) and usually occurs between the ages of 20 and 40 years. All races are affected, but there is a lower incidence in blacks than in whites and Asians (Lee & Ananthakrishnan, 2011).

Pathogenesis: All symptoms of hyperthyroidism are caused by the elevated amount of circulating thyroid hormones that trigger an increase in the **basal metabolic rate** (BMR) (the amount of oxygen consumed while at rest) of each cell resulting in hyperfunction of the cells and excessive body heat production. The results are clearly seen in the clinical manifestations of this disorder.

Extraoral Characteristics: The person with long-standing hyperthyroidism typically presents with the general physical characteristics listed in Table 7.5 (Lee & Ananthakrishnan, 2011; Rubin et al., 2012; Porth, 2011). One-third or more of those with Graves disease will present with some degree of ocular pathology associated with hyperthyroidism. **Exophthalmos,** or protruding eyes, is caused by edema of the muscles and tissues behind the eyeball and is a distinctive feature of this disorder (Fig. 7.11).

Thyroid storm or crisis is a rare life-threatening emergency associated with a hyperactive thyroid that may be seen in patients with undiagnosed, poorly controlled, or

TABLE 7.5 Clinical Manifestations of Hyperthyroidism

System	Manifestation
Nervous	Anxiety, nervousness, tremors of the hand, emotional instability, hyperactivity, insomnia, fatigue, heat intolerance
Integumentary	Warm, smooth, thin skin that may be flushed; hyperhidrosis; may exhibit edema and reddening of the skin of the lower legs; hair is thin, fine, and silky.
Cardiovascular	Increased heart rate and output, palpitations, hypertension, atrial dysrhythmia, congestive heart failure, left ventricular hypertrophy
Gastrointestinal	Increased peristalsis and decreased water absorption in the intestines leads to diarrhea; significant weight loss, increased appetite.
Reproductive	Women: oligomenorrhea or scanty menstrual flow, amenorrhea Men: impotence, decreased libido
Musculoskeletal	Increased muscle activity, large muscle weakness; increased bone resorption, but decreased bone density is normally only seen in postmenopausal women.
Pulmonary	Increased respiratory rate and dyspnea
Blood	Decreased levels of cholesterol

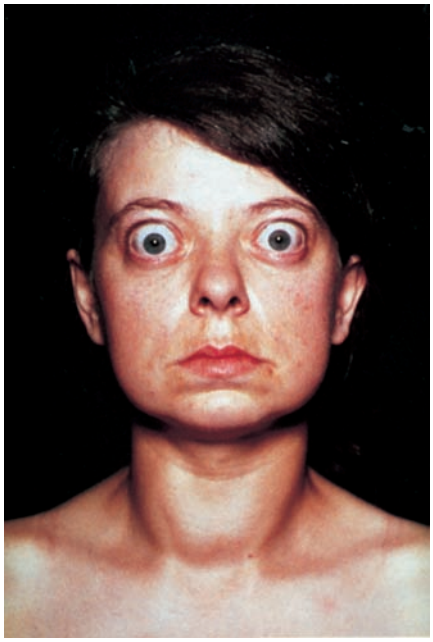

FIGURE 7.11. Hyperthyroidism (Graves disease). A young woman with hyperthyroidism with a mass in the neck and exophthalmos. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

inadequately treated disease. It is normally triggered by an infection, such as influenza, or some sort of trauma and manifests with extreme symptoms of fever, tachycardia (rapid heartbeat), angina (heart pain), and central nervous system effects, such as seizures and psychoses (Porth, 2011).

Perioral and Intraoral Characteristics: Intraoral manifestations in children include early exfoliation of the primary dentition and early eruption of the permanent teeth. Adults have an increased risk of **dental erosion,** loss of hard tissue due to acids not associated with bacterial metabolism, and an increased risk for the development or progression of periodontal disease and/or caries. Burning mouth syndrome (Chapter 10) is more common in these individuals as is osteoporosis of the maxilla and mandible (Chapter 10) (Regezi et al., 2008).

Distinguishing Characteristics: The most obvious clinical manifestation of hyperthyroidism is exophthalmos. However, exophthalmos does not occur in every case and hyperthyroidism must be confirmed with laboratory tests. In addition, as in hypothyroidism, a goiter may be present.

Significant Microscopic Features: Not applicable

Dental Implications: Oral problems associated with hyperthyroidism should be identified and treated aggressively. Topical fluoride should be used frequently at home to help prevent erosion and caries. Early exfoliation of the primary teeth and early eruption of the permanent teeth should be monitored. Symptoms of burning mouth syndrome should always prompt a referral to a physician if the cause cannot be identified. Dental treatment modifications include caution using drugs containing epinephrine and atropine, which are contraindicated in poorly controlled hyperthyroidism because of the potential for causing thyroid storm, and using stress reduction protocols during treatment (Regezi et al., 2008).

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment for hyperthyroidism is focused on decreasing the amount of thyroid hormone available to the cells. Certain drugs can interfere with the production of these hormones or with their use by the cells, or the gland or portions of it can be removed surgically or destroyed by radioactive iodine injected into the blood stream. In almost all cases, treatment for hyperthyroidism results in a lifetime need for thyroid hormone replacement therapy. The prognosis is excellent if treated in a timely manner. Untreated hyperthyroidism can result in congestive heart failure, vision loss, musculoskeletal defects, and untimely death.

Parathyroid Gland

The parathyroid glands are found on the posterior surface of the thyroid gland. There are normally 4 small glands, 2 on each lobe of the thyroid, 1 in a superior position, and 1 in an inferior position, but as many as 12 have been reported (Rubin et al., 2012). The parathyroid glands in conjunction with the parafollicular cells of the thyroid gland regulate the level of calcium in the circulation. While up to 99% of the body's calcium is found in bone and dental tissues, the remaining circulating calcium is essential to the proper functioning of muscles, including the heart, and blood clotting mechanisms. Specialized receptors in the parathyroid gland monitor the level of calcium in the blood, and when it drops below a specific level, the gland releases parathyroid hormone (PTH). PTH stimulates release of calcium from bone, increases reabsorption of calcium within the kidney, and stimulates the production of vitamin D within the kidney. Vitamin D facilitates the absorption of calcium through the intestine. Disorders of the parathyroid glands are associated with hypofunction or hyperfunction of the glands.

Hypoparathyroidism

The most common cause of hypoparathyroidism is removal of the glands during surgical removal of the thyroid (Gonzalez-Campoy, 2012). Hypoparathyroidism can also be inherited as an element of a multiglandular syndrome or, rarely, by itself. DiGeorge syndrome (Chapter 4) is associated with agenesis of the parathyroid glands. Decreased levels of PTH cause hypoparathyroidism, which results in hypocalcemia or a low level of calcium in the blood. The symptoms of hypocalcemia include hyperexcitable muscle tissues or muscle spasms (**tetany**), **hyperreflexia** (exaggerated reflexes), convulsions, and

respiratory muscle spasms, which could be severe enough to cause asphyxiation and death. When young children are affected, the developing dentition undergoes hypoplastic changes that can result in pitting of the enamel and abnormal tooth form or number. Treatment is focused on maintaining an adequate blood calcium level with calcium and vitamin D replacements.

Hyperparathyroidism

There are two main types of hyperparathyroidism, primary and secondary. The most common cause of primary hyperparathyroidism is a single adenoma (benign neoplasm) of unknown cause. Hyperparathyroidism has also been associated with an autosomal dominant inheritance pattern and is seen in multiple endocrine neoplasia syndromes 1 and 2A (discussed in Chapter 17). Parathyroid cancer is rare but does account for some primary cases. Secondary hyperparathyroidism is associated with chronic kidney disease and may also be seen in intestinal malabsorption syndromes such as celiac and Crohn disease (see Chapter 10) and vitamin D deficiency.

Excess PTH causes increased resorption of bone, increased reabsorption of calcium from the kidney, and increased production of vitamin D. Findings in the musculoskeletal system include bone pain, bone demineralization, pathologic fractures, and muscle weakness. Kidney stones tend to develop in these individuals because of the high level of calcium in the circulation, or **hypercalcemia** (Rubin et al., 2012). Demineralization in the maxilla and the mandible may present as generalized thinning and loss of trabecular detail as seen on radiographs or with a cystic appearance due to replacement of the bone with fibrous tissue. Demineralization associated with this disorder is often observed in panoramic radiographs, which can be helpful for diagnostic purposes if this condition is suspected. The lamina dura may be partially or completely absent, a finding that should elicit a referral to a physician for evaluation if noted on radiographs. The teeth may loosen, and in the case of chronic renal disease, the pulp and canals may become completely calcified.

The treatment for hyperparathyroidism depends on the cause and severity of the symptoms. Adenomas can be surgically removed; vitamin D deficiencies can be reversed, and malabsorption syndromes and chronic kidney disease can be managed or controlled. Medical treatment for those with minor or no symptoms would include monitoring blood calcium and PTH levels, limiting calcium intake, and drastically increasing fluid intake.

Adrenal Gland

The adrenal gland is made up of two very different parts: (1) the medulla and (2) the cortex. The medulla forms the inner part of the gland and works in conjunction with the sympathetic nervous system. The medulla secretes epinephrine (adrenaline) and norepinephrine, both of which are also produced within the nervous system. The adrenal cortex forms the outer portion of the gland and is responsible for the production of steroid hormones that are essential for the maintenance of health and life itself. Table 7.6 describes these hormones and their actions. This text concentrates on disorders affecting the adrenal cortex because they are more germane to the clinical practice of dental hygiene. Disorders of the adrenal cortex usually manifest with symptoms caused by either excessive or insufficient levels of the hormones it secretes.

NAME: Adrenocortical Insufficiency

Etiology: *Primary adrenal insufficiency,* or *Addison disease,* is a chronic disorder occurring when cortical hormones are deficient and ACTH levels are elevated because the feedback system is not functioning. Autoimmune destruction of the gland is the most common cause of the disorder in the United States at this time; however, in years past, tuberculosis was the major cause of adrenal destruction in the United States and is still the major cause worldwide (Marzotti & Falorni, 2004; Speiser & Wilson, 2010). Other causes of adrenal destruction include cancer metastasis, histoplasmosis infection, hemorrhage associated with anticoagulants, opportunistic infections associated

APPLICATION **7.1**

Steroid Abuse

No discussion of steroid hormones is complete without mentioning steroid abuse, specifically anabolic–androgenic steroids that are produced in the adrenal cortex. Anabolic–androgenic steroids are used to treat hypogonadism in males, which manifests as a decrease in testosterone production by the testes. Adequate amounts of testosterone are required for normal growth, development, and sexual development and functioning. Anabolic–androgenic steroids are also used to treat some forms of impotence and delayed puberty, to counteract the effects of corticosteroids, to treat anemia that does not respond to normal therapies, and to combat some types of body wasting seen in disorders such as AIDS. Anabolic steroids also cause an increase in skeletal muscle growth and a decrease in body fat.

Steroid abusers desire the latter effects. Weight lifters were the first to start using anabolic steroids to stack the deck in their favor during competitions, but participants in all types of sports are abusing anabolic steroids at this point. Even middle and high school students are abusing these drugs. In a 2011 study entitled "Monitoring the Future," middle and high school students in the United States were surveyed, and an estimated 0.7% of eighth graders, 0.9% of tenth graders, and 1.2% of twelfth graders were found to have taken anabolic steroids at least once (Johnston et al., 2012).

APPLICATION 7.1 (*continued*)

This number has been decreasing since 2001. There are no data on anabolic steroid use in adults, but it is suspected that hundreds of thousands of individuals aged 18 and over are abusing. Males are more likely to abuse steroids than females (NIDA, 2009).

Anabolic steroids have a number of adverse effects seen in both sexes including heart disease, high blood pressure, stroke, high cholesterol, kidney cancer, liver tumors and cancer, depression, eating disorders, increased risk of blood-borne diseases related to using injectable steroids and a nonsterile technique, and acne. Gender-specific undesirable effects include the following:

Males

- Shrinking of the testicles
- Reduced sperm count
- Infertility
- Male pattern baldness
- Gynecomastia (breast development)
- Increased risk for prostate cancer

Females

- Growth of facial hair
- Loss of scalp hair
- Amenorrhea
- Deepening of the voice
- Enlargement of the clitoris

Teenagers who take anabolic steroids before they have completed their vertical growth phases risk never attaining their height potential. Some of these effects are reversible, but the longer one abuses steroids, the more likely these will become permanent.

Aggressive behavior and property crimes (theft and vandalism) appear to be common among steroid abusers. Study results are ambiguous about whether these behaviors are associated with the steroid itself or with the media attention to this type of behavior as being associated with steroid abuse. While abusers usually state they feel good about themselves while on the drugs, depression, thoughts of suicide, and violent mood swings commonly occur when the drug is stopped.

Over-the-counter supplements touted to promote muscle growth and strength can be found in health food stores and pharmacies across the country. These supplements contain a number of metabolic precursors to testosterone including androstenedione, androstenediol, norandrostenedione, norandrostenediol, and dehydroepiandrosterone (DHEA), which are naturally converted into testosterone or similar substances within the body. There is no evidence they promote muscle growth, and they may have long-term side effects associated with their use. Extreme care should be taken by individuals using one of these supplements (DEA, 2004).

Both adults and adolescents who try these drugs may report their use to the dental professional who should be aware of their effects and be prepared to discuss their use when indicated. Individuals who report the use of any of the precursor compounds could be attempting to increase their muscle growth and strength and might be open to a discussion about the effects of anabolic steroids on their general health. Above all, the dental professional should be cognizant of the cardiac problems associated with steroid use and be prepared to use treatment modification strategies to prevent emergency situations.

TABLE 7.6 **Hormones of the Adrenal Cortex**

Classification	Specific Hormone	Function(s)
Mineralocorticoids	Aldosterone	Regulates electrolyte balance by causing kidneys to reabsorb sodium and secrete potassium
Glucocorticoids	Cortisol, cortisone, corticosterone	Acts as a cardiac stimulant Induces the release of vasoconstrictive substances Regulates carbohydrate, lipid, and protein metabolism Inhibits the effects of insulin Increases red blood cell and platelet levels Acts as a strong anti-inflammatory agent
Androgens	Dehydroepiandrosterone (DHEA)[a], androstenedione[a]	Promotes maturation of sex organs Promotes secondary sex characteristics Causes spermatogenesis Maintains various tissues including nervous, skeletal, muscle, skin, and hair
Estrogen	Estradiol, estrone, estriol	Promotes maturation of sex organs Promotes secondary sex characteristics Maintains the menstrual cycle and pregnancy Maintains bone density Causes various metabolic effects on numerous systems

[a]Converted to testosterone in peripheral tissues.

with acquired immune deficiency syndrome, and trauma. Rarely, Addison disease can be associated with an autosomal recessive genetic trait.

Secondary adrenal insufficiency occurs as a result of hypothalamic and/or pituitary disorders or, more commonly, the sudden withdrawal of ingested or injected steroids. Refer to the information on the pituitary gland listed previously for a review of the disorders associated with hypofunction of this gland.

Method of Transmission: In cases other than inherited types, this disorder is not directly transmitted. However, infections causing Addison disease (e.g., tuberculosis, histoplasmosis, and cytomegalovirus) can be transmitted from person to person.

Epidemiology: Primary adrenal insufficiency is a rare disorder with an estimated incidence of 1 per 8,000 individuals (Marzotti & Falorni, 2004). It occurs equally among women and men and tends to be diagnosed between the ages of 30 and 50 years. Secondary adrenal insufficiency is much more common and is estimated to affect over 6 million people in the United States (Klauer, 2009).

Pathogenesis: All of the symptoms of Addison disease are related to deficiencies in hormones the adrenal cortex secretes. Secondary adrenal insufficiency is related to pituitary or hypothalamic dysfunction or suppression of production of glucocorticoids due to therapeutic steroid use. When an individual is taking therapeutic doses of steroid for a medical condition, the adrenal glands stop or slow production of the steroid and atrophy because the pituitary is no longer sending out ACTH. After withdrawal of the steroid, it takes sometimes up to 12 months or longer for the pituitary to recover and release ACTH and for the glands to begin production of enough cortisol to achieve an adequate blood level (Porth, 2011). Medically supervised withdrawal of these drugs is accomplished with doses decreasing gradually over several days or longer, depending on the length of treatment; if it is not done gradually, hypoadrenalism or adrenal insufficiency will occur.

Extraoral Characteristics: Addison disease presents with weakness and fatigue, weight loss, abdominal pain, diarrhea or constipation, and syncope or fainting (loss of consciousness and postural tone due to decreased cerebral blood flow). Almost all individuals will exhibit hyperpigmentation of the skin (referred to as "bronzing"), which gives the individual a tanned look in exposed areas and in areas affected by friction from clothing or function (Fig. 7.12). Elevated levels of ACTH stimulate melanocytic production of melanin, which causes the discoloration. Hyperpigmentation does not occur with secondary adrenal insufficiency because there is no elevation of ACTH in this disorder. **Hypoglycemia,** low blood glucose level, is another common side effect of adrenal insufficiency, and patients must eat regularly scheduled meals to maintain blood glucose levels.

FIGURE 7.12. Addison disease. Hyperpigmentation of the skin over the joints of the hands characteristic of Addison disease. (From Fleisher GR, Ludwig S, Baskin MN. Atlas of pediatric emergency medicine. Philadelphia: Lippincott Williams & Wilkins, 2004.)

Perioral and Intraoral Characteristics: Addison disease causes hyperpigmentation of the gingival and mucosal tissues and the skin of the face. The color of the gingival/mucosal tissues may range from brown to black or even blue (Fig. 7.13).

Distinguishing Characteristics: Hyperpigmentation of the skin and gingival and mucosal tissues is a distinguishing feature of Addison disease but not of secondary adrenal insufficiency.

Significant Microscopic Features: Not applicable

Dental Implications: Hyperpigmentation of the oral and perioral tissues should make the dental professional suspect the presence of the primary disorder. In addition, pigmentation of recent origin could be important and might alert the practitioner to the possibility of the disease. Symptoms of weakness, weight loss, and abdominal pain coupled with a history of steroid use would also alert the dental professional to a possible secondary insufficiency. Both instances require a referral to a physician for evaluation.

Differential Diagnosis: Not applicable

FIGURE 7.13. Addison disease. Oral mucosal hyperpigmentation.

Treatment and Prognosis: Treatment for Addison disease includes replacement of the deficient glucocorticoids with hydrocortisone and maintenance of adequate electrolyte levels in the blood. Secondary adrenal insufficiency also requires hormone replacement therapy until the cause of the problem is corrected, if at all possible. Chronic adrenal insufficiency can be a fatal disease if left untreated; when treated, there is every expectation for a normal life.

Acute Adrenal Insufficiency or Adrenal Crisis

Acute adrenal insufficiency, or adrenal crisis, is a life-threatening condition caused by a sudden physiologically stressful event, such as surgery or trauma, in an individual with chronic adrenal insufficiency. The symptoms are associated with altered electrolyte balances due to mineralocorticoid deficiency and include weakness, vomiting, abdominal pain, confusion, low blood pressure, tachycardia, and lethargy. Vascular collapse, loss of consciousness, coma, and death will result if this condition is not identified and corrected immediately.

Patients with primary Addison disease have the highest risk for this emergency. Patients taking long-term steroid therapy also have a higher risk for this emergency. While the risk for adrenal crisis is usually low in patients taking long-term steroid therapy, those patients taking high-dose therapy (above 50 mg of prednisolone) have a higher risk than those on a low-dose therapy (between 5- and 7-mg prednisolone) (Gibson & Ferguson, 2004). Adrenal crisis can be prevented in the dental environment by obtaining a complete medical and dental history as well as a medication history that includes questions regarding steroid use, length of treatment, and dosage. Medical consultation may be considered if the patient is taking or has taken doses of at least 20 mg/day for 5 days or longer within the last 12 months (Kirkland, 2010). In these cases, supplemental steroids may be needed to create an adequate level of steroid in the blood to avoid an adrenal crisis when dental care, such as extensive surgical procedures, or dental conditions, such as extensive infection, may put undue or unusual stress on the individual. Routine dental and simple surgical procedures do not require supplemental steroids (Gibson & Ferguson, 2004).

NAME: Hyperadrenalism (Cushing syndrome)

Etiology: Cushing syndrome is usually caused by the use of oral, inhaled, topical, or injected steroids for the treatment of medical conditions, in which case it is called exogenous Cushing syndrome. Otherwise, it is caused by endogenous factors such as hypersecretion of ACTH by tumors of the pituitary gland, malignant tumors not of glandular origin (such as small cell carcinoma of the lung), and tumors secreting corticotropin-releasing hormone that stimulate the production of ACTH. Both forms are characterized by the same symptoms and clinical manifestations.

Method of Transmission: Not applicable

Epidemiology: There are no reliable statistics related to the number of cases of exogenous Cushing syndrome caused by the medical use of steroids. The prevalence of this syndrome depends on the frequency and number of conditions requiring this type of therapy occurring in the population being studied. Endogenous Cushing syndrome is a rare disorder affecting about 13 per 1 million individuals in the United States. Most of these cases are due to tumors of the pituitary or adrenal gland. More women than men have these tumors, and they usually occur between the ages of 25 and 40 years (Adler, 2011). Most nonglandular tumors producing ACTH are related to small cell lung cancers.

Pathogenesis: The manifestations of Cushing syndrome are caused by the hypersecretion of ACTH, which causes hypersecretion of the adrenal cortex hormones or hypersecretion of the steroid hormones themselves by the adrenal cortex.

Extraoral Characteristics: The classic *cushingoid* features include increased fat in the abdomen, above the clavicles, and in the upper back (often referred to as a "buffalo hump" Fig. 7.14). Thinning or atrophy of the skin, rapid weight gain, and collagen deficiencies cause purple **striae,** or stretch marks, to form over the abdomen, upper arms, lower back, buttocks, upper thighs, and breasts. Long-term Cushing syndrome can lead to osteoporosis, diabetes mellitus, and stomach ulcers. Other problems include an inability to metabolize glucose effectively, leading to

FIGURE 7.14. Cushing syndrome. Excess fat over the upper back is a classic sign of Cushing syndrome. (Credit: McConnell TH. The nature of disease pathology for the health profession. Philadelphia: Lippincott Williams & Wilkins, 2007.)

FIGURE 7.15. Cushing syndrome. Woman with Cushing syndrome associated with the long-term use of corticosteroid medications. (From Rubin R, Strayer DS, et al. Rubin's pathology: clinicopathologic foundations of medicine. 6th ed. Philadelphia: Lippincott Williams & Wilkins, 2011.)

hyperglycemia (high blood glucose levels), hypertension (Chapter 8), atherosclerosis (Chapter 8), and muscle weakness and wasting. Neurologic findings include depression, emotional instability, and vision abnormalities. Patients may also exhibit steroid acne (on the face, chest, and upper back) caused by an increase in male sex hormones. Women will see an increase and coarsening of facial hair and may see increased hair growth on the neck, chest, and abdomen. Both men and women may experience thinning of scalp hair following male pattern baldness. In addition, Cushing syndrome causes severe growth retardation and lack of sexual development in children.

Perioral and Intraoral Characteristics: Individuals with Cushing syndrome have a very round full face (moon face) caused by edema (Fig. 7.15). They have a higher risk of developing oral and oropharyngeal fungal infections, usually *Candida albicans*, than those without the disorder because of the excessive glucose in the oral tissues and fluids associated with hyperglycemia (Mann, 2003).

Distinguishing Characteristics: None of the characteristic manifestations of Cushing syndrome are pathognomonic for this disorder, although obesity and moon face are the most common features. Medical testing is needed to determine a definitive diagnosis because these physical findings can be attributed to many types of disorders. The most compelling finding would be the use of steroids to treat a medical condition.

Significant Microscopic Features: Not applicable

Dental Implications: Any dental care should be prefaced by obtaining a complete medical/dental and drug history. Steroid drug therapy is used for many common disorders or conditions some of which are listed in Box 7.2. Past and present steroid use should be investigated thoroughly to prevent problems associated with inadequate levels of glucocorticosteroid that might occur during stressful dental surgeries and other treatments (acute adrenal crisis). Medical consultation might be necessary to ensure the well-being of the patient. Patients presenting with oral fungal infections should be treated aggressively with antifungal agents over the course of 10 to 14 days. Air polishing with a sodium bicarbonate–based polishing agent is contraindicated for patients with Cushing syndrome, because the acid–base balance may be disrupted when the bicarbonate is introduced into the circulation (Mann, 2003).

BOX 7.2 Disorders and Conditions Commonly Treated with Corticosteroid Medications

- Arthritis
- Asthma
- Cystic fibrosis
- Eczema
- Hypersensitivity reactions
- Kidney disease
- Leukemia
- Lichen planus
- Organ transplants
- Rheumatoid arthritis
- Sarcoidosis
- Seizures
- Systemic and discoid lupus erythematosus

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment of Cushing disease focuses on the removal of the cause. Surgery to remove pituitary tumors and adrenal tumors is the treatment of choice. As a last resort, complete removal of the adrenal glands could be necessary. Cushing syndrome due to steroid therapy is managed by adjusting dosage amounts, modifying delivery systems to lower systemic exposure, and introducing nonsteroidal drug therapy to limit the use of steroids.

Untreated Cushing syndrome carries a high risk of morbidity from the effects of excess glucocorticoid hormones on the body and premature death (Adler, 2011).

Pancreas

The pancreas functions as both an exocrine and an endocrine gland. As an exocrine gland, it produces and secretes (via ducts) digestive enzymes that reduce the acidity of food substances in the duodenum (the first segment of the small intestine), creating an alkaline environment (pH) for proper digestive enzyme function. The endocrine function takes place in the islets of Langerhans, where hormones having a regulatory effect on the metabolism of carbohydrates, fat, and protein metabolism are produced and secreted into the bloodstream. The hormones of the pancreas and their actions are listed in Table 7.7.

Diabetes mellitus, the most common disorder of the endocrine pancreas, is made up of a group of metabolic disorders characterized by abnormal levels of blood glucose or hyperglycemia, which result in chronic disorders of the small vessels and capillaries (**microangiopathy**), nerves

TABLE 7.7 **Pancreatic Hormones**

Hormone	Islets of Langerhans Cells	Function(s)
Insulin	Beta	Facilitates the entrance of glucose into muscle, fat, and other cells Stimulates the liver to produce glycogen from glucose Decreases glucose concentration in the blood Promotes the synthesis of fatty acids in the liver Decreases the breakdown of fat in adipose tissues Increases the uptake of amino acids Makes many cells more permeable to potassium, magnesium, and phosphate
Amylin	Beta	Slows nutrient uptake
		Suppresses glucagon secretion after eating
		Increases feelings of fullness or satiety
Glucagon	Alpha	Increases blood glucose by stimulating the formation of glucose from glycogen in muscle and fat tissues and in the liver
Somatostatin	Delta	Regulates α- and β-cell function in the islets by decreasing the secretion of insulin and glucagon

(**neuropathy**), and/or large vessels (**macrovascular** disease). Hyperglycemia is due to one or both of the following:

- Failure of the β (beta) cells to produce insulin
- Inability of the body to use the insulin produced, due to insulin resistance in muscle, liver, and fat cells

Diabetes mellitus is separated into several etiologic classifications as seen in Table 7.8. The American Diabetes Association estimates 8.3% of the population or about 25.8 million people in the United States have diabetes (CDC, 2011). Of these, approximately 27% or about 7 million people are not aware they have the disease. Type 2 diabetes accounts for most of the undiagnosed cases. In addition, approximately one in three children born in the year 2000 will develop diabetes at some point in their lifetime (Narayan et al., 2003). Prediabetes statistics are equally dismal with an

TABLE 7.8 **Diabetes Mellitus: Types and Subclassifications**

Type	Subclassification
Type 1 β-cell destruction, usually leading to absolute insulin deficiency	Immune mediated Idiopathic
Type 2 May range from predominantly insulin resistant with relative insulin deficiency to a predominantly secretory defect with insulin resistance	None
Other types	Genetic defects of β-cell function Genetic defects in insulin action Diseases of the exocrine pancreas Other endocrine diseases ■ Acromegaly ■ Cushing syndrome ■ Hyperthyroidism ■ Others Drug or chemically induced Infections ■ Congenital rubella ■ Cytomegalovirus Uncommon forms of immune-mediated diabetes Other genetic syndromes sometimes associated with diabetes ■ Down syndrome ■ Turner syndrome ■ Klinefelter syndrome
Gestational diabetes mellitus	None

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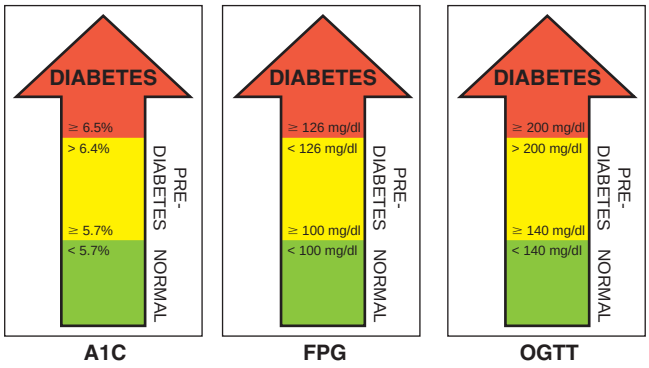

FIGURE 7.16 Hemoglobin A1C, fasting plasma glucose, and OGTTs. Glucose levels associated with normal, prediabetic, and diabetic metabolic states for each of the three tests. (Copyright 2012 American Diabetes Association, from http://www.diabetes.org. Reprinted with permission from The American Diabetes Association.)

estimated 79 million Americans aged 20 or older with prediabetes in 2010 (CDC, 2011). The incidence of the different types of diabetes is as follows (Khardori, 2012):

- Type 1, 5 to 10%
- Type 2, 90 to 95%
- All others except gestational diabetes, 1 to 5%

There are three tests available to diagnose either diabetes or **prediabetes** (blood glucose levels higher than normal but not yet high enough to be considered diabetes): (1) the **fasting plasma glucose test** (FPG), (2) the **oral glucose tolerance test** (OGTT), or (3) the **glycated hemoglobin test** (A1C). The results of these tests indicate whether the patient has a normal metabolism, prediabetes, or diabetes. Diabetes is present when the results of these tests indicate hyperglycemia (see Fig. 7.16). There are four primary forms of diabetes dental professionals will encounter: type 1, type 2, prediabetes, and **gestational diabetes mellitus** (glucose intolerance first detected during pregnancy). The characteristics of each are discussed in the following sections.

NAME: Diabetes mellitus type 1

Etiology: β-cells in the islets of Langerhans are destroyed by an autoimmune process associated with a strong genetic predisposition. There are no known risk factors for type 1 diabetes, and it cannot be prevented at this time.

Method of Transmission: Type 1 immune-mediated diabetes has been shown to have a relatively strong genetic predisposition involving genes associated with human leukocyte antigens (HLA) among others (Porth, 2011; Rubin et al., 2012; Kidambi & Patel, 2008).

Epidemiology: Type 1 diabetes occurs more frequently in whites and least frequently in Asians. It can occur at any age but develops primarily in children, adolescents, and young adults (CDC, 2011). Overall, cases have been increasing in number every year both in the United States and worldwide.

Pathogenesis: Currently, autoimmune destruction of the β-cells in the islets of Langerhans is considered the major factor in the pathogenesis of type 1 immune-mediated diabetes. Approximately 90% of the β-cells must be destroyed before insulin levels drop enough to cause the blood glucose level to increase (hyperglycemia) and the disease to become clinically apparent. Many patients present first as medical emergencies before being diagnosed (see "Diabetic Ketoacidosis" below).

The classic symptoms of diabetes are polydipsia, polyuria, and **polyphagia** (excessive hunger). High blood glucose levels (hyperglycemia) lead to excessive water loss through the urine (polyuria), which leads to dehydration and intense thirst (polydipsia). Insulin is necessary for the metabolism of glucose; therefore, a deficiency of insulin will cause the individual to feel hungry all of the time (polyphagia). Persistent hyperglycemia affects all organ systems leading directly to the chronic complications associated with diabetes. Several mechanisms have been proposed to explain the cellular damage associated with diabetes. One involves free radical injury; another involves the activation of a substance called protein kinase C or PKC that plays a role in increasing insulin resistance and proliferation of endothelial and smooth muscle cells (Rubin et al., 2012). Another mechanism involves the process of **glycosylation** where glucose normally binds to proteins, lipids, and nucleic acids in a reversible manner. In individuals with diabetes, chronic hyperglycemia leads to permanent binding of glucose to these substances causing changes in their structure and function. The substances (proteins, lipids, etc.) changed by this process are collectively called **advanced glycation end products** (AGE) and are thought to contribute to the thickening of the endothelial basement membranes characteristically seen in diabetes (Rubin et al., 2012). Glucose also binds with hemoglobin molecules in red blood cells, forming the basis for one of the most accurate tests currently available to assess an individual's control of his or her diabetes over a period of time (glycemic control).

The **hemoglobin A1C** test measures how much glucose binds to **HbA1c** (a specific type of hemoglobin) during the life of the red blood cell and is currently considered to be the best measure of glycemic control. Box 7.3 describes this test more fully. Most individuals with diabetes are accustomed to determining their blood glucose levels, measured as milligrams per deciliter of blood (mg/dL), several times a day; they often have difficulty understanding the relationship of the A1C to their daily glucose levels. Recognizing this, the American Diabetes Association has developed a method to convert the A1C percentage to an **estimated average glucose** (eAG) number that uses the same unit of measurement (mg/dL) seen on lab reports and the patient's own meter (Nathan et al., 2008). This method of reporting the patient's A1C result is better understood and patients can more easily identify a daily goal to work toward in achieving glycemic control. Table 7.9 lists guidelines for evaluating A1C results and notes the corresponding eAG values.

BOX **7.3** **Glycated Hemoglobin (A1C) Test**

Glycosylation is the basis for the glycated hemoglobin test, which measures the amount of glucose bound to molecules of hemoglobin A1C. When red blood cells are formed, they do not contain any glucose. As the red blood cells move through the circulatory system, glucose molecules become attached to the hemoglobin contained within them in the process known as glycosylation. The higher the level of glucose in the blood, the more glucose molecules become attached to the hemoglobin within the red blood cells. Once the glucose is attached to the hemoglobin, it stays attached. The amount of glucose bound to the hemoglobin reflects the average level of glucose the cell has been exposed to over time (60 to 80 days; see Table 7.9). This is a very accurate method of tracking individuals' control of their glucose levels during the 2 to 3 months prior to the blood test and has been found to be a better predictor of diabetic microvascular complications than the daily blood glucose testing all patients with diabetes should be performing. The A1C test is the gold standard for assessing glycemic control and is now approved for use in diagnosing diabetes.

Extraoral Characteristics: Individuals who have type 1 diabetes are often thin or of normal weight. They usually present initially with polydipsia, polyuria, and polyphagia. Those with untreated type 1 diabetes may experience a dramatic weight loss in a relatively short period of time (days or weeks), even if eating more than normal, because they are unable to use glucose or convert it into fat. They may exhibit flu-like symptoms of weakness and fatigue, frequent infections, and slow wound healing. The onset of symptoms is abrupt and often manifests as diabetic ketoacidosis (DKA), which can quickly lead to death if not treated. The complications associated with diabetes can be separated into acute and chronic manifestations of the disease. The acute manifestations of type 1 diabetes are associated with short-term fluctuations in blood glucose levels and include hypoglycemia and DKA, a severe form of hyperglycemia.

- Hypoglycemia. Hypoglycemia usually results from having too much insulin **(hyperinsulinism).** Hypoglycemia, sometimes called *insulin reaction* or *insulin shock,* is common in type 1 diabetes (may be seen infrequently in type 2 diabetes) and is related to taking too much insulin, eating too little food, or underestimating the amount of glucose needed in specific situations such as strenuous exercise or during extremely stressful events. Unfortunately, individuals who successfully maintain a close to normal blood glucose level are more frequent victims of this condition than those who do not control their disease as well. This happens because tight control gives little room for miscalculating the amount of insulin needed for the amount of food ingested. Therefore, if the patient's glucose levels have even minor fluctuations, hypoglycemia will result. Symptoms of hypoglycemia usually occur when glucose levels fall below 60 to 45 mg/dL of blood. If untreated, hypoglycemia results in altered consciousness, coma, and death. In addition, some individuals with diabetes may experience **hypoglycemic unawareness** and become unconscious before they have any idea their glucose levels are low. This condition is seen more often in patients who have very tight control of their glucose levels, take certain heart or blood pressure medications such as β-blockers, or have neuropathy. It is also very common in young children, especially under the age of 5, who lack the cognitive ability to interpret the warning signs of hypoglycemia (NDEP, 2011). Frequent episodes of hypoglycemia have been associated with permanent cognitive impairment in children under the age of 5 (NDEP, 2011).
- **Diabetic ketoacidosis.** DKA is a result of excessive hyperglycemia and occurs when the body must break down fat to use as an energy source instead of glucose. Fat metabolism results in increased levels of circulating fatty acids, which stimulate the liver to produce ketones that build up in the blood and cause **acidosis** (a decrease in the pH of the blood). Acidosis causes altered consciousness, coma, and eventual death if not treated.

Table 7.10 compares hypoglycemia and DKA with **hyperosmolar hyperglycemic state** (HHS), the acute manifestation associated with type 2 diabetes (discussed later in this chapter).

TABLE **7.9** **Interpreting A1C Results**

A1C Percentage	Estimated Average Glucose (mg/dL)	Interpretation
<5.7%	<117	Normal
5.7–6.4%	117–137	Prediabetes
<6.5%	140	A1C criteria for diagnosis of diabetes; may be considered a target treatment level for select individuals without a history of frequent hypoglycemia
<7%	<154	Target treatment level for most patients with diabetes
<8%	154–182	Target treatment level for some patients with a history of frequent hypoglycemia, short life expectancy, or coexisting medical conditions
>8%	>183	Poor control; the physician should be working with the patient to improve glucose levels.

TABLE 7.10 Comparison of Hypoglycemia, Ketoacidosis, and Hyperosmolar Hyperglycemic State (HHS)

		Hyperglycemia	
	Hypoglycemia	**Diabetic Ketoacidosis (DKA)**	**HHS**
Associated with	Type 1	Type 1	Type 2
Blood glucose levels	<60 mg/dL	>250 mg/dL	>600 mg/dL
Speed of onset	Very fast	Gradual, many hours to several days	Occurs more gradually than ketoacidosis, but the manifestations often have a fast onset.
Symptoms	Altered behavior Altered consciousness Anxiety Coma Cool, clammy skin Headache Hunger Impaired mental ability Polydipsia Sweating Tachycardia	Acetone or fruity breath odor Polydipsia Polyuria Nausea Tachycardia Increased rate and depth of respirations Vomiting Dry mouth Fatigue Headache Hypotension Coma	Aphasia (impaired communication capabilities) Coma Dehydration Hyperthermia Hypotension Nausea Polydipsia Seizures Tachycardia Unilateral paralysis Vision blurring Vomiting Weakness Weight loss
Emergency care	Oral or intravenous glucose	Call EMS	Call EMS

Diabetes affects every organ in the body, and the chronic complications associated with it occur slowly over many years. A direct relationship exists between the incidence of complications and the patient's control of their blood glucose and cholesterol levels and blood pressure. The American Diabetes Association reports less than 10% of patients with diabetes achieve all three of the following treatment goals (ADA, 2012):

- A1C level less than 7%
- Blood pressure less than 130/80
- Cholesterol levels less than 100 mg/dL

Given the preventive health philosophy of dental practices, dental professionals should be aware of these complications and be able to recognize the need for a prompt medical referral. Complications are not reversible, but disease progression can be slowed or prevented. A listing and brief description of the most common complications are provided below.

- *Neuropathy.* Approximately 60 to 70% of those with diabetes will experience neuropathy (nervous system damage). **Peripheral neuropathy** is the most common manifestation and may present as loss of sensation or pain in the lower legs, feet, or hands. **Autonomic neuropathy** affects the autonomic nervous system and results in gastrointestinal problems such as delayed emptying of the stomach, causing slow digestion of food in type 1 diabetes, and gastroesophageal reflux disease (Chapter 10) in type 2 diabetes. Neuropathy can also be associated with symptoms normally related to repetitive stress injuries such as carpal tunnel syndrome (CDC, 2011). Fluctuations in blood glucose levels have been linked to cognitive impairment such as confusion and delayed decision making, and there is some evidence Alzheimer disease may be associated with diabetes because nerve tissue in the brain produces small amounts of insulin (Odetti et al., 2005; Rivera et al., 2005).
- *Microangiopathy.* Microvascular changes include thickening of the capillary basement membranes, hyperplasia of the endothelium, and thrombosis or blood clots. These changes cause **retinopathy** (retinal disease), **nephropathy** (kidney disease), and skin and joint problems. Microangiopathy has also been implicated in the initiation and progression of periodontal infections (see the section on "Infections" and Application 7.2). Diabetic retinopathy is the leading cause of blindness between the ages of 20 and 74 in the United States (CDC, 2011) and results when capillaries in the retina hemorrhage and cells in the retina become hypoxic causing fibrous tissue to replace normal tissues in the retina and optic disk. Nephropathy is the result of tissue damage caused by hyperglycemia and the creation of AGEs during glycosylation, among other events. The exact mechanism is unknown, but the end result is sclerosis (hardening) of the glomeruli and kidney failure. Diabetes is the leading cause of kidney failure and end-stage kidney disease in the United States (CDC, 2011). Microangiopathy is also a factor in the development of **diabetic dermopathy,** which presents as chronic red, hyperpigmented, papular, well-circumscribed, oval

APPLICATION **7.2**

Diabetes, Periodontal Disease, and Oral/Systemic Health

The dental hygiene profession has a special interest in how diabetes affects the periodontal health of an individual. There is strong evidence establishing diabetes as a risk factor for gingival and periodontal disease, and periodontal disease has been identified by many as the sixth complication of diabetes (Loe, 1993; Persson, 2011; Lamster et al., 2008). Research also supports findings that uncontrolled diabetes (consistent A1C levels of greater than 9%) plays an important role in the development and progression of periodontal disease. Data suggest that periodontal disease in those with diabetes is not only related to the impaired host response described below but also to the same biologic mechanisms that cause other classic diabetic complications, such as the microvascular changes associated with retinopathy and kidney disease (Mealey & Oates, 2006; Persson, 2011).

The body normally mounts a defense when gingival tissues are challenged by the organisms found in dental biofilm; this defense is impaired in diabetes. Defective polymorphonuclear neutrophils (PMNs) are slow to respond to chemotactic factors or they do not respond at all. They also do not recognize the pathogens and are often unable to phagocytize them. In addition, macrophages and monocytes appear to be hyperresponsive in individuals with diabetes, because AGEs, which are present in the periodontal tissues, are able to recruit more of these cells into the area and activate them, increasing their ability to cause extensive destruction of both normal and diseased tissues (Mealey & Oates, 2006; Porth, 2011). AGEs can also stimulate the production of excessive amounts of chemical mediators such as interleukin-β (Il-1β), prostaglandin E_2, and tumor necrosis factor-α (TNF-α). These substances accumulate in the soft tissues, causing additional tissue destruction and increased inflammation (Lyle, 2003; Mealey, 2004; Southerland, 2005; Mealey & Oates, 2006). Increased tissue destruction and decreased ability of the body to repair periodontal tissues are linked to altered collagen production in diabetes, including (1) a decrease in the growth of fibroblasts, (2) a decrease in their ability to produce collagen, and (3) an increase in collagenase activity. In addition, osteoblasts exhibit a decreased ability to produce bone matrix, which also leads to increased amounts of periodontal bone loss.

Microangiopathy occurs when AGE-modified collagen accumulates in the endothelial cells of the small vessels, causing thickening of the basement membranes, which leads to impaired nutrient supply and endothelial cell changes, which are linked to clot formation (Mealey & Oates, 2006; Southerland, 2005). These microvascular changes further compromise the periodontal tissues and exacerbate the destructive process (see Application Table).

Researchers have been investigating other aspects of the periodontal disease–diabetes link, including whether periodontal disease could be a predictor of future type 2 diabetes. Demmer et al. (2008) used data from the first National Health and Nutrition Examination Survey (1971 to 1976) and at least one follow-up evaluation (1982 to 1992) to look at whether the presence of periodontal disease could predict, independently of other factors, incidents of diabetes twenty years later. They concluded that in the almost 10,000 individuals without diabetes enrolled in the original study, severe periodontal disease was a predictor of developing type 2 diabetes. They concluded this information would be of great public health significance if it could be confirmed through further study because periodontal disease is a preventable and treatable condition. A second study done by Demmer et al. in 2008 found even more evidence of an association between periodontal disease and increasing A1C levels in a population without diabetes, again suggesting periodontal disease may be a contributing factor for the development of type 2 diabetes. Regular dental care may be

Diabetes-Related Changes Believed to be Associated with the Development and Progression of Periodontal Disease

Diabetes Complication	Specific Action	Effect on Periodontium
Impaired PMN function	Decreased chemotaxis Decreased adherence Decreased phagocytosis	Decreased host response
Impaired collagen production	Decreased growth of fibroblasts Decreased production of collagen by fibroblasts	Decreased healing/repair and impaired ability to maintain periodontal tissues
Increased collagenase production	Increased collagen destruction	Increased tissue destruction and decreased healing/repair
Impaired bone formation	Decreased production of bone matrix by osteoblasts	Decreased ability to maintain periodontal bone levels
Presence of AGEs	Increases recruitment of macrophages and monocytes Activates macrophages and monocytes to the area Increases production of IL-1 and TNF-α Associated with microangiopathy	Enhanced destruction of periodontal tissues
Microangiopathy (pathological changes in the small vessels)	Increased likelihood of blood clot formation Increased thickness of the capillary basement membrane	Impeded blood flow to the periodontium and compromised transfer of nutrients necessary to maintain tissue health

(continued)

APPLICATION 7.2 (*continued*)

associated with fewer emergency visits and hospital admissions related to diabetes. In a study by Mosen et al. (2012), regular dental care was associated with a lower number of diabetes-specific emergency department visits and hospital admissions. The authors did not find a similar association between regular dental care and control of diabetes as measured by A1C levels (Mosen et al., 2012).

Links between diabetes and other conditions have been suggested by other studies. A study by Meisel et al. (2010) found a higher-than-normal risk of developing oral leukoplakia in those with diabetes. In addition, they reported that the risk for developing oral leukoplakia continually rose as A1C levels increased above normal and, not surprisingly, they found the risk to be even higher in those with diabetes who smoked. Studies have also shown a correlation between increasing periodontal disease activity with exacerbation of diabetic retinopathy and cardiovascular disease.

Individuals with diabetes do not have to suffer from periodontal disease. Those who have good control of their diabetes and adequate oral hygiene have no more risk of developing the disease than those without diabetes. However, those with consistent A1C levels of greater than 9% (CDC, 2011) have a significant risk of developing periodontal disease. Dental professionals have a responsibility to maintain current knowledge of diabetes and the oral–systemic link in order to provide optimal care and education for our patients.

lesions. These are usually found on the shins but may be found on the thighs and forearms (Fig. 7.17).

- *Macrovascular disease.* Macrovascular disease presents as coronary artery disease, peripheral vascular disease, and/or stroke (Chapter 8). Atherosclerosis is the major cause of these disorders and is less associated with chronic hyperglycemia than it is with glycosylated proteins and lipids or other AGEs, elevated triglyceride and cholesterol levels, and increased clotting often seen in diabetes. Coronary heart disease occurs two to four times more often in those with diabetes than in the general population and accounts for about 68% of deaths related to diabetes (CDC, 2011). Peripheral vascular disease is also related to high blood pressure, atherosclerosis, and resulting occlusion of the small vessels of the lower extremities. Peripheral vascular disease often results in gangrene (necrosis due to loss of blood supply) and amputation. Diabetes is a major cause (60%) of lower extremity amputations not due to trauma (CDC, 2011). Those with diabetes are two to four times more likely to have a stroke than the general population (CDC, 2011). Strokes, or cerebrovascular accidents, are associated with hypertension, atherosclerosis, and thrombosis, all of which are related to diabetes.

FIGURE 7.17. Diabetic dermatopathy. Small, brownish, atrophic, scarred, hyperpigmented plaques are seen on the shins. (From Goodheart HP. Goodheart's photoguide of common skin disorders. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

- *Infection.* Chronic and recurring infections and impaired wound healing are other complications of diabetes. The higher risk of infection in patients with diabetes is associated with a decreased host response thought to be due to the following factors among others:
  1. Decreased blood supply because of microangiopathy, resulting in a decrease in the number of white blood cells and nutrients (including oxygen) that are brought to the areas at risk of infection
  2. Impaired white blood cell function (WBCs fail to function at glucose levels over 200 mg/dL) resulting in decreased adherence, chemotaxic and phagocytic functions (Porth, 2011; Clement et al., 2004)
  3. Increased bacterial and fungal growth supported by a hyperglycemic environment
  4. Decreased vision and sense of touch increase the risk of trauma to the extremities.

  Specific infections have a tendency to occur more often in patients with diabetes. These include skin infections (bacterial and fungal), oral and periodontal infections (bacterial and fungal), osteomyelitis (bone infection), urinary tract infection, and kidney infection and may reactivate tuberculosis (Rubin et al., 2012; Porth, 2011; Khardori, 2012). Infection in any area makes it hard to control glucose, usually requiring an increase in the amount of insulin taken to maintain a normal level; chronic infections can make consistently maintaining a normal blood glucose level almost impossible.

- *Musculoskeletal problems.* Research supports a relationship between diabetes and musculoskeletal problems, including accelerated age-related changes to the

connective tissues and joints resulting in mobility problems (Craig et al., 2008). Nearly 30% of patients under the age of 28 with type 1 diabetes have limited joint mobility (LJM) of the small and large joints exacerbated by thickened skin overlying the joints (Kim et al., 2001). A simple test to determine LJM, called the **prayer sign,** involves the patient placing his or her hands in the position seen in Figure 7.18 and noting how much contact is obtained between the opposing fingers as shown. Patients with LJM will not be able to obtain good contact. This type of LJM may affect home care procedures and the patient's ability to control oral infections. In addition to joint problems, studies confirm bone mineral density (BMD) is lower in patients with type 1 diabetes than those of the same age and sex without diabetes, resulting in an increased risk of hip fractures almost twice that of those without diabetes (Brown & Sharpless, 2004). **Osteopenia** (decreased bone density) or **osteoporosis** (significantly decreased bone density) is not associated with type 2 diabetes. However, the risk of hip fracture remains high due to impaired vision, poor balance, loss of sensation in the lower extremities, and limited joint mobility (Brown & Sharpless, 2004). Decreased bone density is a predisposing factor for periodontal bone loss.

- *Epithelial changes.* High levels of insulin are thought to stimulate the proliferation of epidermal keratinocytes and dermal fibroblasts causing thickening and hardening of the skin, especially over joints.
- *Psychosocial issues.* Depression is twice as likely to occur in patients with diabetes as opposed to those without diabetes (De Groot et al., 2010). Bulimia or binge eating behaviors are seen in from 3.8 to 27.5% of patients with type 1 diabetes. If you consider insulin withholding as a form of eating disorder, the estimate is 38 to 40% (Young-Hyman, 2010). Omitting or reducing the daily insulin dose is a form of weight control used predominately by adolescent and young adult women, allowing them to eat but not utilize the glucose in the food. In other words, they intentionally create a very dangerous hyperglycemic state that can lead to significant long-term complications.

Box 7.4 lists the chronic complications of diabetes.

Perioral and Intraoral Characteristics: Several oral conditions have been associated with diabetes; most are seen in individuals unable to maintain consistently good control of their blood glucose levels. The most destructive of these manifestations is periodontal disease (Fig. 7.19). Individuals with diabetes are two to three times more likely to not only have periodontal infections but also have more severe infections than someone without diabetes (CDC, 2005; Mealey,

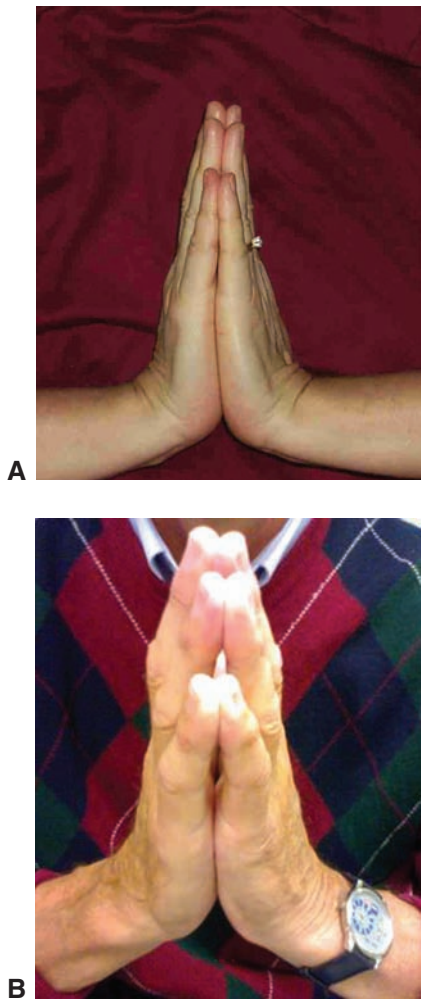

FIGURE 7.18. Prayer sign. **A.** Normal contact attained between the palms of hands and fingers. **B.** This individual with diabetes is unable to achieve normal contact. (Courtesy of Dr. Perttu Arkkila.)

BOX 7.4 Chronic Complications Associated with Diabetes

Neuropathy	Peripheral neuropathy Autonomic neuropathy
Microvascular changes	Retinopathy Blindness Nephropathy Kidney failure Foot problems Ulcerations Charcot foot (bone deformities) Periodontal disease
Macrovascular changes	Atherosclerosis Coronary artery disease Thrombus formation Peripheral vascular disease Amputation of lower extremities Stroke Hypertension
Musculoskeletal changes	Limited joint mobility Skin thickening Decreased connective tissue elasticity
Altered host response	Infection Periodontal disease Skin Urinary tract

FIGURE 7.19. Periodontal involvement. Periodontal disease associated with uncontrolled diabetes and local factors.

2004; Faria-Almeida et al., 2006). Refer to Application 7.2 for more information on periodontal disease and diabetes. Other oral changes often seen in diabetes include parotid gland enlargement (Fig. 7.20) with possible xerostomia, burning mouth syndrome (Chapter 10), increased risk for multiple periodontal abscesses, and an increased incidence of fungal (*C. albicans*) infections (Chapter 14). Not surprisingly, patients who have poor control of their diabetes may exhibit a higher rate of caries than those who have better control.

FIGURE 7.20. Parotid gland enlargement. Parotid gland enlargement and xerostomia are often associated with diabetes. (Courtesy of Dr. Frank Varon.)

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: A medical referral is appropriate to evaluate a patient who presents with oral signs of periodontal infection, fungal infection, and/or multiple periodontal abscesses in addition to a suspicious medical history, advancing age, and obesity, especially for patients who have been in the practice for a length of time and have never had such manifestations. Under these circumstances, suspicion of diabetes is not unreasonable because of the large number of individuals with undiagnosed disease in the population. Glucose levels for all patients with diabetes should be determined by use of a glucometer prior to initiating any dental/dental hygiene assessment or treatment procedures. Glucose levels below 80 mg/dL should be corrected to avoid hypoglycemia before continuing with the appointment. A glucose source should be kept close at hand during the appointment in case glucose levels drop suddenly. Patients who have high glucose levels should be referred to their physician for medical management to achieve their optimal level (ADA, 2012). The results of the patient's most recent A1C test should be noted because it indicates how well the patient has controlled his or her diabetes over time and not just at the time of the dental appointment. This percentage is an important indicator of the risk of periodontal disease and predictor of treatment outcome after periodontal therapy. A high risk of periodontal disease is associated with A1C results of greater than 9% (CDC, 2011). Patients with diabetes should have individualized treatment plans focused on customizing their periodontal care and managing oral conditions based on their diabetes status and level of control (Pera, 2011) (refer to Clinical Protocol #16).

Differential Diagnosis: Not applicable

Treatment and Prognosis: Insulin is absolutely necessary in the treatment of type 1 diabetes, and individuals with either type are often on medications to control cholesterol levels and high blood pressure as well. Diet control and exercise programs are also crucial for the management of diabetes. Initially, patients undergo diabetes education by a *certified diabetes educator* (either an RN or dietitian), and a diabetes care plan is prepared for the patient. All should be under strict diet constraints, but this is usually the most challenging aspect of diabetes management and causes the most compliance issues. Age, lifestyle, and individual personality factors have much to do with how well patients adhere to a strict diet. The dental professional has an opportunity to reinforce the dietary plan developed by the diabetes educator and enhance the patient's motivation to stay with a diet program by pointing out all of the oral benefits of maintaining good glucose control.

Type 1 patients should check blood glucose levels at least four times per day and should visit a physician two to four times a year to have their A1C, blood pressure, and cholesterol assessed. Remember, A1C levels of 7% or lower have been shown to lower the incidence of microangiopathy; the incidence of macrovascular disease is also lowered but only if glycemic control (7% or lower) is maintained long-term beginning at diagnosis (Hirsch & Parkin, 2005; ADA, 2012). In addition, it is extremely important for these individuals to have annual dilated eye examinations; pregnant women should have a dilated eye examination during their third trimester. Regular foot examinations should be done by a physician or a podiatrist.

The core diabetes care team includes the physician (endocrinologist, family practitioner, internal medicine) and the diabetes educator with consulting health care specialties including dentistry, podiatry, cardiology, physical therapy, occupational therapy, pharmacology, neurology, and gastroenterology to name a few. Patients who use their diabetes care team will possess the tools to control their disease. However, many patients do not take advantage of this resource. The dental professional has the opportunity to ask patients about their medical care and about how they manage their diabetes (refer to Clinical Protocol #16).

Oral problems treated without first addressing overall diabetes management issues usually have less than optimal treatment outcomes. Dental hygiene treatment should stress thorough periodontal debridement with as little trauma as possible. Patients with diabetes have a high risk of developing periodontal abscesses; therefore, complete periodontal debridement should be accomplished in one area before moving on to another area or tooth. Treatment of xerostomia, burning mouth syndrome, and fungal infections should be aggressive, with steps taken to prevent recurrence or long-term effects. Oral infections can have a severe impact on diabetes control for several reasons; for example, products created by the inflammatory response can increase insulin resistance, making control harder, and patients may be unable to follow a proper diet because of oral pain.

Over 225,000 people with diabetes die each year from diabetes-related complications, making diabetes the seventh leading cause of death in America (CDC, 2011). Research is providing hope for preventing diabetes. Studies on rats found mechanisms that interfere with the autoimmune destruction of the islet cells in the pancreas, thereby allowing the islet cells to regenerate. If this can be replicated in humans, islet cell destruction could be stopped (Bresson et al., 2006).

NAME: Diabetes mellitus type 2

Etiology: Type 2 diabetes is a multifactorial disease with a strong genetic predisposition and many recognized risk factors including obesity (abdominal), family history of type 2 diabetes, prior gestational diabetes and/or birth of a baby weighing nine or more pounds, impaired glucose metabolism, hypertension, physical inactivity, race or ethnicity (Blacks, Latino, Native American, Asian/Pacific Islander), older age (greater than 45), and low levels of high density lipoprotein (HDL) cholesterol and high levels of triglycerides (CDC, 2011; Porth, 2011; Rubin et al., 2012; ADA, 2012). Polycystic ovary syndrome, which affects 5 to 10% of women of childbearing age, has also been identified as a risk factor for type 2 diabetes because most women with this condition are also insulin resistant and many are obese. Data suggest that type 2 diabetes may be prevented by eliminating as many of these risk factors as possible.

Method of Transmission: Type 2 diabetes is associated with a strong genetic predisposition (Porth, 2011; Rubin et al., 2012; ADA, 2012; Khardori, 2012).

Epidemiology: As stated above, 90 to 95% of those with diabetes have type 2 diabetes. In addition, most of the people who are unaware they have diabetes have type 2 diabetes. Type 2 diabetes occurs more frequently in Hispanics, Native Americans, Blacks, and Asian/Pacific Islanders than in non-Hispanic Whites. It also occurs more often after the age of 40 and increases significantly after the age of 60. However, type 2 diabetes is being seen more frequently than ever before in young people, especially in the ethnic groups listed above, in part due to the alarming rise in childhood obesity and inactivity that crosses all racial and ethnic boundaries (ADA, 2012).

Pathogenesis: Type 2 diabetes occurs because of decreased sensitivity or increased resistance to insulin in the target cells, located in the liver, skeletal muscle, and adipose tissues. Obesity, diet, and lack of exercise are the main cause**s** of insulin resistance. Persistent hyperglycemia, caused by poor glycemic control, stimulates the pancreas to produce ever-increasing amounts of insulin to lower blood glucose. Eventually, the β-cells are literally worn out and undergo apoptosis (natural cell death). The pathogenesis of the complications associated with hyperglycemia in type 2 diabetes is essentially the same as for type 1, and the reader is referred to that section for review. Many individuals with type 2 diabetes can decrease the severity of their disease or eliminate it altogether by losing weight and significantly increasing their activity level.

Extraoral Characteristics: Ninety percent of individuals who have type 2 diabetes are overweight or obese (Khardori, 2012). The classic signs of polydipsia, polyuria, and polyphagia may not be present in this form of diabetes. The symptoms associated with type 2 diabetes are often vague, and since they progress slowly from mild to more severe over time, it is possible they might go unnoticed by the patient and health care providers. A patient may have diabetes for 4 to 7 years before a diagnosis is made and very often have varying degrees of retinopathy, neuropathy, or nephropathy at the time of diagnosis (Khardori, 2012). Recurrent infections, nonhealing sores, visual changes,

APPLICATION **7.3**

Obesity

Approximately one-third of all Americans over the age of 20 (35% of women and 31% of men) and 12.7 million or 17% of children and adolescents between 2 and 19 are obese (CDC, 2011). Not included in this statistic are individuals who are overweight but not yet considered obese who could number in the millions. Many in health care feel obesity is the most important public health issue this nation has ever faced. Obesity in adults is defined as a body mass index (BMI) of 30 or more, while overweight is defined as a BMI of 25 to 29.9 (CDC, 2011). BMI for children is calculated using an age- and sex-specific chart; overweight children fall in the 85th to 94th percentile for their age and sex, while the 95th percentile or greater defines childhood obesity. Obesity has a multifactorial etiology, which includes elements associated with inheritance, environment, culture, behavior, and socioeconomic status. However, in most cases, and simply stated, obesity is caused by ingesting too many calories and not getting enough exercise (CDC, 2011). The CDC estimates $147 billion dollars were spent on direct (health care, etc.) and indirect (sick days, etc.) costs associated with obesity in 2008. The number of health problems associated with being obese is increasing as research uncovers more information every day, including cardiovascular disease, type 2 diabetes, insulin resistance, breast and colon cancers, hypertension, high cholesterol and triglycerides, stroke, liver and gall bladder disease, respiratory problems and sleep apnea, osteoarthritis, early puberty, infertility, and polycystic ovaries (see Application 3.1).

Behavioral and environmental factors are the focus for most prevention and treatment activities. Improving nutrition by increasing consumption of fruits and vegetables and decreasing consumption of sugary drinks (sports drinks, soda, flavored drinks), high-energy-dense foods (protein bars, candy), and increasing physical activity by limiting television viewing time and encouraging walking or other activity on a daily basis are both effective strategies for losing weight or maintaining a healthy weight (CDC, 2011). Individuals who struggle with a weight problem should seek the advice of a health care professional to determine the best program for their specific needs.

With over one-third of the population considered overweight or obese, dental professionals will be seeing more of these individuals as time passes. Strict adherence to office protocols for obtaining accurate medical/dental and drug histories as well as reviewing histories to assess changes in risk associated with cardiovascular and metabolic disease at every appointment should alert dental personnel to the need for appointment modifications or additional oral risk assessments. Patients may need more frequent maintenance appointments, nutritional counseling, and health education focused on the oral–systemic link and strategies to modify risk factors. Patients might need to be referred to a registered dietitian for intense nutrition counseling or to a periodontist if indicated by the severity of periodontal disease present (Spolarich, 2009). The dental hygienist is in an excellent position to offer information, encouragement, and help in achieving and maintaining a lifestyle that will establish both general and oral health.

and numbness in the extremities are significant findings suggesting type 2 diabetes. The acute manifestations of type 2 diabetes are hypoglycemia and HHS, discussed below:

- *Hypoglycemia*. The symptoms associated with hypoglycemia in type 2 diabetes are much more subtle than those seen in type 1 diabetes and are usually due to not eating enough or engaging in excessive activity. The patient may exhibit a mild behavior or mood change; he or she may feel light-headed and hungry.
- ***Hyperosmolar hyperglycemic state.*** HHS, although uncommon, is seen in patients with type 2 diabetes. It manifests with high levels of blood glucose that cause severe dehydration, low blood volume, and low blood flow to vital organs. Severe dehydration leads to coma and death (11% of cases) if not reversed (Kitabchi et al., 2006). HHS is seen more often in older persons who have a concurrent illness that causes reduced fluid intake, such as an infection.

Table 7.10 summarizes and compares the acute complications associated with type 1 and type 2 diabetes. The chronic complications of type 2 diabetes are essentially the same as those associated with type 1 diabetes (see Box 7.4).

Perioral and Intraoral Characteristics: Perioral and intraoral characteristics are similar for both type 1 and type 2 diabetes (refer to this section under type 1 diabetes). Interestingly, type 2 diabetes is often associated with a higher risk of caries than type 1 diabetes due to the high-carbohydrate diet associated with obesity, which is characteristic of this condition.

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: It is important for dental professionals to be aware of the risk factors for type 2 diabetes and to recognize them when reviewing a medical history prior to treatment. If prediabetes or type 2 diabetes can be present for 4 to 7 years before being diagnosed, it is possible the dental professional might recognize some of the characteristic signs and initiate a referral that could result in earlier treatment and delay or elimination of some chronic complications. Patients with sudden changes in oral health such as increased inflammation, bleeding, and higher levels of caries, especially without a change in oral hygiene, might be exhibiting signs indicative of diabetes. A referral to a physician may be indicated for these patients especially if these signs occur in the presence of other identified

diabetes risk factors. Many dental practices are checking blood glucose levels of patients they suspect may have diabetes or prediabetes and referring them to physicians for evaluation when results are abnormal (Radmer et al., 2009). For more information, refer to Dental Implications under Diabetes mellitus type 1 and to Clinical Protocol #16.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Type 2 diabetes is normally treated with oral medications that increase the amount of insulin the pancreas produces, decrease the resistance of the cells to the action of insulin, or increase insulin sensitivity within the cells. Insulin may be used to treat type 2 diabetes if it becomes necessary. Patients with type 2 diabetes should check their blood glucose levels at least twice a day. Otherwise, the management of type 2 diabetes is essentially the same as management of type 1 diabetes. The prognosis for those with type 2 diabetes is directly related to their level of glucose control and the number and severity of chronic conditions present.

NAME: Prediabetes

Prediabetes always precedes the development of type 2 diabetes. Prediabetes is a warning sign, a predictor of things to come if the individual does not do something to modify or eliminate risk factors.

Etiology: Genetic and environmental factors have a strong influence on the development of type 2 diabetes; therefore, these same factors will influence the development of prediabetes.

Method of Transmission: Type 2 diabetes is associated with a strong genetic predisposition.

Epidemiology: In the United States, there are 79 million people, age 20 years or older, who have prediabetes (CDC, 2011). The ethnic groups with the highest risk for type 2 diabetes also have the highest risk for prediabetes.

Pathogenesis: The pathogenesis of prediabetes is identical to that of type 2 diabetes. Prediabetes may be present for 4 to 7 years or more before it progresses to diabetes. Recent research has shown that chronic damage to the body, especially the heart and circulatory system, may occur during prediabetes (American Diabetes Association, 2006). In addition, research has shown that early intervention to manage blood glucose levels during the period of prediabetes may delay or prevent the development of type 2 diabetes.

Extraoral Characteristics: **Acanthosis nigricans,** or hyperpigmentation of the skin of the neck, axillae, and groin areas (Fig. 7.21), is a clinical finding used to screen for prediabetes or high risk for type 2 diabetes. Acanthosis nigricans is associated with high levels of insulin, obesity, diabetes, and other endocrine disorders and may present prior to any overt sign of disease, making recognition of this entity during the head and neck examination important for making a prompt medical referral. Otherwise, the characteristics of prediabetes are similar to those of type 2 diabetes.

FIGURE 7.21. Acanthosis nigricans. Hyperpigmentation and thickening of the skin at the nape of the neck is characteristic of prediabetes. (Courtesy of Dr. Frank Varon.)

Perioral and Intraoral Characteristics: Identical to those of type 2 diabetes

Distinguishing Characteristics: Patients will have a blood glucose level that is higher than normal but not yet high enough to be considered type 2 diabetes.

Significant Microscopic Features: Not applicable

Dental Implications: All of the oral problems associated with type 1 or 2 diabetes may manifest in these patients. Recognition of an individual at risk of prediabetes and prompt referral may prevent chronic complications from developing (see Dental Implications under Diabetes mellitus type 2).

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment usually consists of dietary and lifestyle changes. These individuals have a substantial risk of developing type 2 diabetes and the associated chronic complications. Losing weight and starting an exercise program that includes moderate-intensity physical activity are essential elements of preventing type 2 diabetes (CDC, 2011).

Gestational Diabetes Mellitus

Gestational diabetes mellitus (GDM) is glucose intolerance that is first detected during pregnancy. GDM is seen in from 2% to 10% of all pregnancies in the United States (CDC, 2011). Risk factors for developing gestational diabetes include a family history of diabetes, delivery of large or heavy babies, five or more pregnancies, older age and obesity, as well as being of an ethnic origin associated with a higher risk for type 2 diabetes. GDM usually manifests after the major fetal morphogenic events (organ development, etc.) have occurred; therefore, the effects of gestational diabetes on the fetus differ from those seen in pregnancies in which the mother has type 1 or 2 diabetes. In GDM, glucose in the blood crosses the placenta and enters the fetal circulation. If there is too much glucose, a state of hyperglycemia is produced, and in response, the fetal pancreas starts producing more insulin to lower the glucose level. However, the fetus does not need that much energy for its metabolic functions, and the excess glucose is stored as fat. This is the reason for the exceptionally large babies born to these mothers. In addition, babies born with excess insulin have a higher risk of being obese children and of developing type 2 diabetes as adults. Treatment for GDM focuses on nutritional management and physical activity. If these measures do not bring the glucose level under control, insulin injections will be prescribed. GDM will subside with declining pregnancy hormone levels. However, approximately 5% to 10% of women who have GDM will present with type 2 diabetes after their pregnancy has ended. In addition, women who have had GDM have a 35% to 60% chance of developing type 2 diabetes within 10 to 20 years (Moore, 2012). GDM patients require medical follow-up for 2 years postpartum.

SUMMARY

- The nervous and endocrine systems are responsible for regulating the many functions of the body. The nervous system is responsible for immediate actions; the endocrine system is responsible for slower processes.
- The endocrine system is composed of glands that secrete hormones or chemical messengers directly into the blood or lymph systems without using any ducts.
- Hormones are received by target cells with receptors for the hormones on their cell membranes.
- The hypothalamus receives information from the nervous system and the body and directs the pituitary to release the proper hormones to maintain body functions.
- The endocrine system is regulated by a negative or positive feedback system. The negative feedback system stops the release of a specific hormone when it senses that there is an adequate level of that hormone in the circulation. The positive feedback system releases one hormone based on the rising level of another hormone and stops releasing that one hormone when the level of the other hormone drops.
- Endocrine disorders take many forms, but the symptoms associated with them are usually linked to either hyposecretion or hypersecretion of the specific hormones associated with that gland.
- Diabetes insipidus is caused by a lower-than-normal level of ADH and is not associated with hyperglycemia. Polydipsia and polyuria are characteristic features of this disorder, as is the potential for severe life-threatening dehydration.
- Hypopituitarism or hyposecretion of any of the pituitary hormones will cause hypofunctioning of the gland that is associated with that particular pituitary hormone. The clinical characteristics are identical to those caused by hypofunction of the specific gland without any associated pituitary hypofunction.
- Hypopituitarism is more severe in children because the hormones are needed for proper physical and mental development. Hypopituitarism in adults manifests as premature aging and may result in an acute adrenal crisis.
- Hypersecretion of growth hormone by the pituitary will result in gigantism, if it occurs prior to the end of puberty, or acromegaly, if it occurs after the end of puberty.
- The thyroid gland regulates the body's BMR among other functions. Hyposecretion of the gland causes symptoms associated with a decrease in the BMR in an adult and severe growth and mental deficiencies in children. Hypersecretion causes symptoms associated with a rise in BMR in both adults and children. Uncontrolled hyperthyroidism can lead to a life-threatening condition known as a thyroid storm.
- Goiters are caused by hypertrophy or hyperplasia of the thyroid gland, not neoplastic growth.
- The parathyroid glands regulate the level of calcium in the blood. Hypoparathyroidism causes hyperreflexia and possible hypoplasia of developing teeth. Hyperparathyroidism is associated with musculoskeletal problems, kidney stones, and generalized bone demineralization.
- The adrenal glands produce steroid hormones. Primary adrenal cortical insufficiency, or Addison disease, may present with bronzing of the skin over high-use areas such as the joints and hyperpigmentation of the oral mucosa. Secondary adrenal insufficiency may result from the sudden withdrawal of corticosteroid medications. Hyperpigmentation is not seen in secondary adrenal insufficiency because there is no rise in ACTH. Hypoglycemia is common, and there is a potential for adrenal crisis.

- Hyperadrenalism causes Cushing syndrome due to endogenous (hyperfunctioning gland) or, more commonly, exogenous factors (medical use of steroids). Hyperglycemia is common in hyperadrenalism as are the classic cushingoid features. Adrenal crisis should be anticipated when treating individuals who have a history of corticosteroid use.
- The pancreas has both endocrine and exocrine functions. The endocrine pancreas secretes insulin, which regulates carbohydrate, protein, and fat metabolism. Diabetes mellitus is the most common disorder associated with the pancreas.
- Hypofunctioning of the pancreas due to destruction of the β-cells is known as type 1 diabetes. Type 2 diabetes is caused by increased resistance or decreased sensitivity of the target cells to insulin. Diabetes presents with both acute and chronic manifestations. The chronic manifestations of diabetes cause significant morbidity and mortality, making diabetes the seventh leading cause of death in the United States.
- Prediabetes (type 2 only) is associated with an increased risk of developing diabetes and the chronic complications associated with diabetes.
- Gestational diabetes increases a woman's risk of developing type 2 diabetes after the birth of her child and places the child at risk for developing diabetes.
- Diabetes is associated with a significant risk of developing dental infections including periodontal disease. An inadequate host response coupled with microangiopathy is considered to be the most likely pathogenesis.

CHAPTER REVIEW

Case Study 7.1

Your elderly male patient thinks his face is changing, getting longer and heavier, and he sees increased spacing between his mandibular teeth (Fig 7.22). He has recently been diagnosed with sleep apnea, feels tired all of the time, and recently had to get his rings resized because his fingers are getting fatter. In addition, he complains of repeatedly biting his tongue to the point he thinks it is getting larger and just doesn't fit in his mouth anymore.

1. What are the significant observations the patient has related to you?
2. What endocrine condition are all of these symptoms associated with?
3. What is the most common cause of this condition?
4. What dental problems are associated with this condition?
5. What results if this condition occurs prior to the end of puberty?

FIGURE 7.22. Copyright (C) Kenneth Yamanaka, DDS/CC-BY-SA-3.0 (*http://creativecommons.org/licenses/by-sa/3.0/*). Available at: *http://en.wikipedia.org/wiki/File:Acromegalyteethgapping.jpg*, accessed February 5, 2012.

For answers and additional review activities, log in to **thePoint.lww.com**

Case Study 7.2

A 26-year-old female patient presents for a regularly scheduled preventive dental hygiene appointment. As you update her medical history, she tells you that she has gained about 20 lb in the last 6 months for no reason she can determine; she has continued her level of activity even though she has been extremely tired. During her extraoral examination, you observe what you think is a slight thickening of her neck in the area of the thyroid gland (Figs. 7.23 and 7.24).

1. If you assume this is evidence of a goiter, what type of thyroid dysfunction would you suspect? Why would this cause a goiter?
2. What other history questions could be asked to help determine the type of disorder?
3. What physical symptoms accompany this dysfunction?
4. What oral abnormalities are associated with this type of dysfunction?
5. What is the prognosis of this disorder if treated? If untreated?
6. What is your responsibility as a health care professional in this instance?

FIGURE 7.23.

FIGURE 7.24.

For answers and additional review activities, log in to **thePoint.lww.com**

Critical Thinking Activities

1. Determine your risk factors for type 2 diabetes including sex, age, weight, ethnicity, diet, relatives who have diabetes, activity levels, and any individual factors that might be related to your risk of diabetes. Answer the following questions and discuss them with your classmates.
   - **A.** What are some measures you can take to decrease your risk of diabetes?
   - **B.** What are the risk factors you cannot change?
2. Imagine you have just been told you have type 1 diabetes; what are your first thoughts? What changes do you feel you will have to make to control your diabetes?
3. Are there cultural differences in how a person reacts to having and managing diabetes? If you and your classmates have culturally diverse backgrounds, discuss how this diagnosis would be handled from each of your unique cultural perspectives.
4. Imagine you have just been told your 10-year-old child has type 1 diabetes. What information do you want to receive from your dental health care provider?

Portfolio Possibilities

- Search the Internet and find Web sites to which you can refer patients with diabetes for assistance with oral health, meal planning, exercise programs, and other topics you find interesting. Try to find a variety of sites and organize them into sites for general information, those that might appeal to children or teens, ones appropriate for women or men, some that are specific for type 1 or type 2 diabetes, and possibly sites for pregnant women with GDM. Prepare a patient reference sheet with the sites listed, along with a brief description of the information at the site and the appropriate audience. Distribute these sheets to your patients in your school dental hygiene clinic. You can also use this as a handout when performing community service at health fairs, etc.
- Many dental/dental hygiene schools and private dental offices work with area school sports departments to make mouth guards for their players. Propose adding some steroid abuse, tobacco cessation, and staying quit information to the event. While the players are waiting their turn or waiting for delivery of the mouth guard, you can facilitate a discussion about their experiences and offer information about the substances and how to avoid them. Consider contacting a sports celebrity in your area to add more enthusiasm to the event. Describe the event in your portfolio and reflect on what you learned from the experience.

Media Menu

Web Sites

Center of Excellence for Training and Research Translation – Organization whose mission is to increase the public health impact of programs to prevent obesity, heart disease, stroke and other chronic diseases
http://www.center-trt.org/

DiabetesAtWork.org – Interesting site with resources for educators such as lesson plans and fact sheets
http://www.diabetesatwork.org/index.cfm

Multimedia Resources

Centers for Disease Control and Prevention: The Obesity Epidemic
http://www.cdc.gov/CDCTV/ObesityEpidemic/index.html

The Endocrine System – Excellent review of the system and its functions
http://youtu.be/-S_vQZDH9hY

Study Tools

Take advantage of additional online resources to help you study and ace your exams!

- Answers to case studies in the book
- Additional case studies and answers
- Interactive quiz bank with answer feedback
- Fully searchable e-book for quick look-up and studying on-the-go
- Expanded Media Menu with direct links to related Web sites and multimedia resources
- Supplemental references

thePoint Online resources and links are available at *http://thepoint.lww.com/DeLong2e*

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Chapter 7 **LESION/CONDITION SUMMARY TABLE**

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Diabetes insipidus	Low ADH associated with tumors, head trauma, infections	Low ADH causes dehydration and electrolyte imbalance.	Intense polydipsia, polyuria	N/A	Desmopressin, adequate water intake, low-sodium diet	Xerostomia may be present, if so, expect increased biofilm and caries risk. Makes use of removable appliances difficult; multiple restorations and xerostomia increase home care difficulty.
Hypopituitarism	Pituitary neoplasm	Deficiency of any of the pituitary hormones will cause lower level of the target hormone.	Children: severe development problems related to the specific deficiency, failure to thrive Adults: premature aging, low vital signs, adrenal crises possible	N/A	Removal of the tumor if possible, hormone supplementation for deficient hormones	Delayed eruption of primary and secondary teeth, delayed exfoliation, inform parents of potential for malocclusion
Gigantism (giantism), Acromegaly	Pituitary neoplasm	Hypersecretion of growth hormone causes excessive growth/ enlargement.	Gigantism: excessive growth of the skeletal system prior to puberty resulting in very tall well-proportioned individuals. Acromegaly: enlargement of soft tissues and bones of hands, feet, face, and skull, and possible enlargement of organs and entrapment of nerves in foramina	N/A	Removal of the neoplasm if possible	Malocclusion, poorly fitting prostheses, macroglossia, fissured tongue, possible TMJ dysfunction
Hypothyroidism (Hashimoto thyroiditis)	Worldwide: iodine-deficient diet U. S.: autoimmune destruction	Iodine is necessary for the production of thyroid hormone (T3 and T4). Autoimmune reaction causes destruction of some or all of the thyroid tissues.	Lethargy, memory loss, depression, cold intolerance, edema of face, hands, and feet, dry rough skin, hair loss, decreased vital signs, general weakness, joint pain, anemia, weight gain Puffy lips, enlarged gingiva, macroglossia, delayed eruption of primary and secondary teeth, delayed exfoliation Congenital: Severe growth retardation, lack of development, and mental deficiency	N/A	Eliminating the cause, hormone supplements	Investigate the cause of gingival edema and refer for medical evaluation if indicated; pseudoanodontia due to delayed eruption may indicate need for temporary prosthetic appliance.
Hyperthyroidism (Graves disease)	Autoimmune destruction, infection, neoplasm	Elevated levels of thyroid hormone cause an increase in basal metabolic rate leading to classic symptoms.	Anxiety, tremors, insomnia, heat intolerance, warm smooth skin, thin hair, edema of lower legs, increased vital signs, diarrhea, weight loss, exophthalmos Early exfoliation and eruption of primary teeth and eruption of secondary teeth, dental erosion, high risk of caries and periodontal disease, burning mouth syndrome, osteoporosis	N/A	Eliminating the source of excess thyroid production (surgical removal or radioactive destruction of the gland or tumors), thyroid hormone replacement therapy	Topical fluoride to prevent erosion and caries, monitor eruption and exfoliation of teeth, refer for medical evaluation for osteoporosis or burning mouth syndrome, use caution when giving drugs containing epinephrine or atropine to avoid thyroid storm
Hypoparathyroidism	Removal of the glands, inherited, agenesis of the gland	Low levels of PTH cause hypoparathyroidism resulting in hypocalcemia.	Tetany, hyperreflexia, convulsions, respiratory muscle spasms Enamel hypoplasia, abnormal tooth and root form, abnormal tooth numbers	N/A	Calcium supplementation and vitamin D replacement	Identify the cause of enamel hypoplasia, manage dental problems caused by abnormal formation or number of teeth
Hyperparathyroidism (primary, secondary)	Primary: adenoma, genetic, cancer secondary: renal disease, malabsorption syndromes	Excess PTH causes bone resorption, increased reabsorption of calcium, increased production of vitamin D	Bone pain, bone demineralization, pathologic fractures, muscle weakness, kidney stones (hypercalcemia) Thinning of maxilla and mandible, loose teeth	Generalized thinning of bone, loss of trabecular detail, cyst-like appearance (bone replaced with fibrous tissue), loss of lamina dura, pulp chambers and canals may calcify.	Removal of adenoma, vitamin D supplements, treat/control malabsorption syndromes or renal disease, limit calcium intake and increase fluid intake	Investigate causes for radiographic findings characteristic of hyperparathyroidism and refer for medical evaluation

continues

Chapter 7 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Adrenocortical insufficiency (primary [Addison disease]. secondary)	Primary autoimmune destruction, cancer, infection, hemorrhage, trauma Secondary hypothalamic/ pituitary dysfunction, abrupt withdrawal of ingested steroids	Primary deficiency in hormones creates symptoms. Secondary pituitary or hypothalamic dysfunction or suppression of function due to therapeutic steroid use or abuse	Weakness, fatigue, weight loss, abdominal pain, syncope, hyperpigmentation of skin (Primary only), hypoglycemia Hyperpigmentation of gingiva and mucosa (Primary only) Adrenal crisis: weakness, vomiting, abdominal pain, confusion, low blood pressure, tachycardia, lethargy, vascular collapse unconsciousness, coma, death	N/A	Replacement of deficient glucocorticoids with hydrocortisone Secondary requires replacement of hormones also.	Investigate etiology of oral pigmentations especially of recent origin along with general symptoms for primary disease Look for a history of recent steroid use in the presence of symptoms for secondary disease Obtain a complete medical/dental/drug history including length of steroid therapy and dosage, obtain medical consult if necessary; may need to supplement steroid dose to prevent adrenal crisis
Hyperadrenalism (Cushing syndrome)	Use of oral, inhaled, topical, or injected steroids or hypersecretion of adrenocorticotropic hormone due to benign or malignant neoplasms	Hypersecretion of adrenocorticotropic hormone causing hypersecretion of adrenal cortex hormones or hypersecretion of steroid hormones by adrenal cortex	Abdominal fat, fat above clavicles and in upper back, atrophic skin, weight gain, purple striae over abdomen, upper arms and back, osteoporosis, diabetes mellitus, stomach ulcers, hypertension, atherosclerosis, muscle weakness and wasting, depression, loss of hair, steroid acne Moon face, high risk of oropharyngeal fungal infections	N/A	Surgery to remove tumors, manage medication induced by modifying dosage amounts, delivery systems to decrease systemic exposure, consider the use of nonsteroidal medications	Obtain a complete medical/dental/drug history including length of steroid therapy and dosage, obtain medical consult if necessary, may need to supplement steroid dose to prevent adrenal crisis Oral fungal infections should be treated aggressively with antifungals for 10–14 days; air polishing contradicted.
Diabetes mellitus type 1	Strong genetic predisposition, unknown	Autoimmune destruction of β-cells in islets of Langerhans causes deficiency of insulin and prevents glucose from entering cells causing increased levels of glucose in the blood.	Polydipsia, polyuria, polyphagia; thin or normal weight; slow wound healing, fatigue, weakness, frequent infections Acute: hypoglycemia, hyperglycemia Chronic complications: retinopathy, atherosclerosis, neuropathy, nephropathy, dermopathy, stroke, peripheral vascular disease, coronary artery disease, limited joint mobility, osteopenia/osteoporosis, thickening/hardening of skin, depression, eating disorders Oral: periodontal infections/abscesses, periodontitis, parotid gland enlargement, fungal infections, burning mouth syndrome, xerostomia	N/A	Insulin, diet control, and exercise Medications to control blood pressure and cholesterol Preventive eye, foot, and dental examinations	Refer patients with symptoms suggestive of diabetes to a physician for evaluation Obtain preappointment blood glucose levels to avoid hypoglycemic emergencies, refer patients with high glucose levels to their physicians, obtain most recent A1C test results to determine the level of glycemic control and risk of periodontal and other chronic diseases Perform complete debridement of an area before moving to the next to avoid periodontal abscesses Encourage diet control and exercise as well as optimum oral hygiene Educate patients about the oral–systemic connection between diabetes and periodontal disease and the reverse
Diabetes mellitus type 2	Multifactorial with strong genetic predisposition	Insulin resistance in target cells causes persistent hyperglycemia, which stimulates the pancreas to produce more insulin, eventually destroying β-cells.	Obese or overweight; may see polydipsia, polyuria, and polyphagia but not always; vague, slowly progressive symptoms often not diagnosed for 4–7 years Acute: hypoglycemia, hyperosmolar state Chronic complications: same as for type 1 diabetes Oral: same as for type 1 diabetes	N/A	Oral medications, possible insulin therapy, diet control, and exercise Medications to control blood pressure and cholesterol Preventive eye, foot, and dental examinations	Same as for type 1 diabetes
Prediabetes	Multifactorial with strong genetic and environmental factors	Same as diabetes mellitus type 2	Similar to diabetes mellitus type 2, may exhibit acanthosis nigricans	N/A	Diet and lifestyle changes	Recognize acanthosis nigricans and refer for evaluation Patient education about the long-term complications of diabetes; prevention, obesity, exercise, etc.; and the oral–systemic connection

CHAPTER 8

Cardiovascular Disorders

KEY TERMS

Aneurysm
Angina
Arteritis
Autonomic neuropathy
Carditis
Distal
Dysrhythmia
Embolus/emboli(pl)
Endocardium
Epistaxis
Exsanguination
Heart murmur
Hypercholesterolemia
Infarction
Ischemia
Laminar
Nocturia
Orthopnea
Paroxysmal nocturnal dyspnea
Pathologic murmur
Petechiae
Physiologic murmur
Polycythemia
Pulmonary hypertension
Regurgitate
Shunt
Thrombus
Transient ischemic attack (TIA)
Unstable angina
Ventricular fibrillation

LEARNING OUTCOMES

1. Define terminology used in discussing cardiovascular disorders.
2. State the significance of turbulent blood flow and describe ways in which normal laminar blood flow may become turbulent.
3. Identify the etiology of the disorders discussed in this chapter.
4. Recognize the method of transmission and describe the pathogenesis of the disorders discussed.
5. Describe the characteristics and distinguishing features of cardiovascular disorders.
6. Describe dental implications, including appointment modifications, patient management strategies, and patient education topics for the cardiovascular disorders discussed.
7. Discuss the possible association between oral infections and atherosclerosis.
8. Describe the dental implications of antithrombotic therapy and discuss appointment modifications to manage patients taking antithrombotic medications.
9. Identify cardiovascular conditions that could precipitate a medical emergency in the dental office and describe how to avoid or prevent them, if appropriate.
10. List behavior and lifestyle changes that could be suggested to help control hypertension.
11. Describe the warning signs of stroke and why it is important to get the patient to a medical facility as soon as possible.
12. List potential oral problems associated with stroke and appointment modifications for patients affected by stroke.
13. Identify the most common congenital heart defects.
14. Identify the most common heart valve defect.
15. List heart disorders associated with an increased risk of infective endocarditis.
16. Describe the rationale for giving prophylactic antibiotics to patients with certain heart disorders prior to specific dental procedures.
17. List diseases and disorders that may cause the development of congestive heart failure.
18. Describe the significance of cardiac dysrhythmia.

CHAPTER OUTLINE

The Cardiovascular System
The Heart
The Vessels
Vascular Disorders
Atherosclerosis
Hypertension
Hypertensive Heart Disease
Coronary heart disease (CHD)
Peripheral Artery Disease
Abdominal aortic aneurysm (AAA)
Raynaud disease (primary) and Raynaud phenomenon (secondary)
Thromboembolic venous disorders
Stroke
Heart Disorders
Congenital heart defects
Heart valve defects
Mitral valve prolapse (MVP)
Rheumatic heart disease
Infective endocarditis
Congestive heart failure (CHF)
Dysrhythmias

RELATED CLINICAL PROTOCOLS

#4 Treating Patients with Xerostomia
#17 Oral Health Care Management for the Patient with Heart Disease
#21 Oral Health Care Management for the Patient Taking Anticoagulant Medications

The Cardiovascular System

The cardiovascular system consists of the heart and two distinct circulatory systems: (1) pulmonary circulation, right side of the heart, which carries blood from the heart to the lungs and back to the heart, and (2) systemic circulation, left side of the heart, which carries blood from the heart to the rest of the body and then back to the heart. Within the circulatory systems, arteries take blood away from the heart in progressively smaller vessels until the blood reaches a capillary bed, where nutrient exchange occurs. At this point, the venous system takes over, and the blood flows through progressively larger veins until it is returned to the heart.

The Heart

The heart receives blood from the vena cava into the right atrium. The blood travels through the tricuspid valve into the right ventricle, at which time it enters the pulmonary circulation and is pumped through the pulmonary valve (semilunar) into the pulmonary artery (the only artery carrying nonoxygenated blood) and then into the lungs. The oxygenated blood travels through the pulmonary vein (the only vein to carry oxygenated blood) into the left atrium. The blood is now in the systemic circulatory system. Once the blood is in the left atrium, it is pumped through the bicuspid or mitral valve into the left ventricle. The blood is then pumped through the aortic valve (semilunar) into the aorta and then to the rest of the body (Fig. 8.1). All of the valves are continuous with the **endocardium** (the innermost lining of the heart) and function to prevent backflow. The endocardium is also continuous with the lining of the blood vessels. The electrical stimulation of the heart is regulated by the autonomic nervous system. The impulses begin in the sinoatrial (SA) node in the right atrium and travel to the atrioventricular (AV) node, which lies in the right atrial wall just superior to the tricuspid valve. At this point, the impulses travel through fibers from the AV node to the bundle of His, located in the inferior portion of the ventricular septum, where the fibers split and carry the impulses to the right and left ventricles, terminating in the Purkinje fibers. The heart muscle is provided with oxygen and nutrients through the coronary arteries.

The Vessels

All vessels except the capillaries are composed of three distinct layers: the tunica externa, tunica media, and tunica interna. The tunica externa consists of fibrous tissue that supports the vessel. The tunica media consists mostly of smooth muscle that causes the vessels to constrict or dilate, regulating the amount of blood that is flowing through the vessel and the pressure within the vessel. The tunica interna is the innermost layer, which is composed of an elastic layer that connects the interna with the media and a thin layer of endothelial cells that provide a smooth, slick surface over which the blood flows (Fig. 8.2). Normal blood flow is **laminar,** or layered, with the slower plasma flowing closest to the endothelial layer and the cellular components flowing more quickly within the innermost portion of the vessel. Turbulent blood flow occurs when there is a defect or injury to the vessel or endothelial surface or a change in the amount of pressure within the vessel. Turbulent blood flow allows the blood components to become more mixed with the plasma and increases the chance that platelets and other factors that encourage clotting can come in contact with the endothelium and create a clot, or **thrombus** (Fig. 8.3A and B). In visual terms, imagine normal blood flow like water flowing very evenly in a stream with a smooth, flat sandy bottom; then imagine that same water flowing over rocks, bumping into rocks and swirling in eddies between and behind boulders, that is what turbulent blood flow is like. Blood flows through the vascular system under a certain amount of pressure. The blood pressure within the circulation to the lungs (pulmonary) is low compared with the higher pressure required to move the blood through the systemic circulation. Abnormal variations in blood pressure in either the pulmonary or the systemic circulation can have serious effects, such as cardiac enlargement, valve disorders, and stroke, among others.

Arteries are thick-walled vessels that can handle the high pressure needed to move blood through them to the outermost parts of the body. Veins are thinner-walled vessels

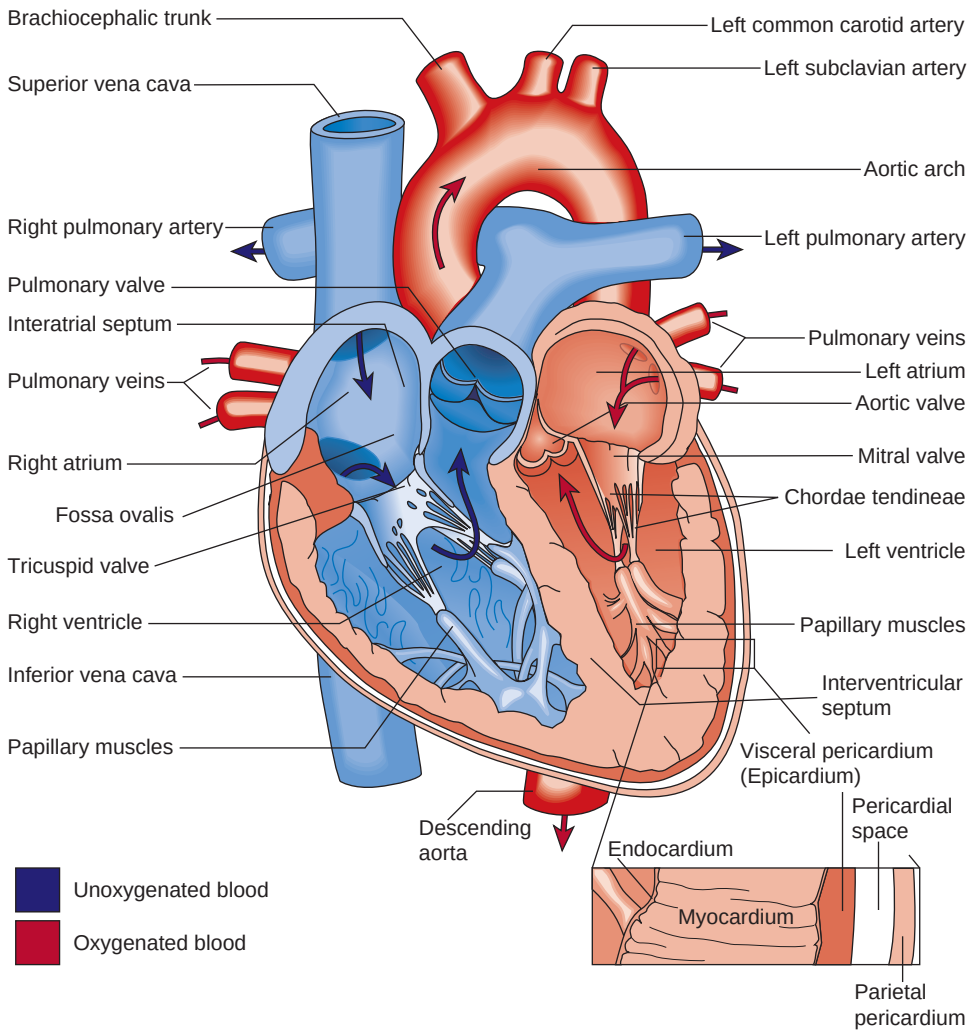

FIGURE 8.1. The heart. Anatomic landmarks and normal blood flow through the heart. (From Smeltzer SCO, Bare BG. Brunner and Suddarth's textbook of medical-surgical nursing. 9th ed. Philadelphia: Lippincott Williams & Wilkins, 2002.)

that do not have to contend with the high pressure associated with arteries. However, veins must work against gravity to bring blood back from the extremities to the heart. Therefore, unlike arteries, veins are equipped with valves that prevent backflow of blood that has already passed through them (Fig. 8.2).

If any of the parts of these systems are compromised by disease or defect, blood will not move efficiently through them, and tissues and organs will not receive the nutrients necessary to maintain health. Vascular system disorders are discussed before disorders of the heart because vascular pathology is involved in the etiology of many heart disorders. In addition, vascular pathology is often caused by heart disorders, making it essential to have an understanding of vascular pathology first.

Vascular Disorders

Abnormalities of the vascular system can be congenital, genetic, or acquired. Most often, they are caused by a combination of genetic and environmental factors. The following sections focus on diseases or disorders of the arteries and veins and abnormal blood pressure.

NAME: Atherosclerosis

Etiology: Atherosclerosis is a disease of the arteries in which inflammatory cells, smooth muscle cells, lipids, and connective tissues accumulate within the tunica interna. The exact cause of atherosclerosis is not clearly understood. It is not known why some individuals live their entire lives without vascular pathology due to atherosclerosis while others have pathology at a very early age. There are both modifiable and unmodifiable risk factors associated with the development of this disease. Risk factors such as increasing age and being male as well as having a family history of atherosclerosis (possibly genetic in origin) cannot be changed or modified by the individual. However, other risk factors strongly associated with this disease such as hypertension, **hypercholesterolemia** (high cholesterol), cigarette smoking, physical inactivity, and high stress levels can be

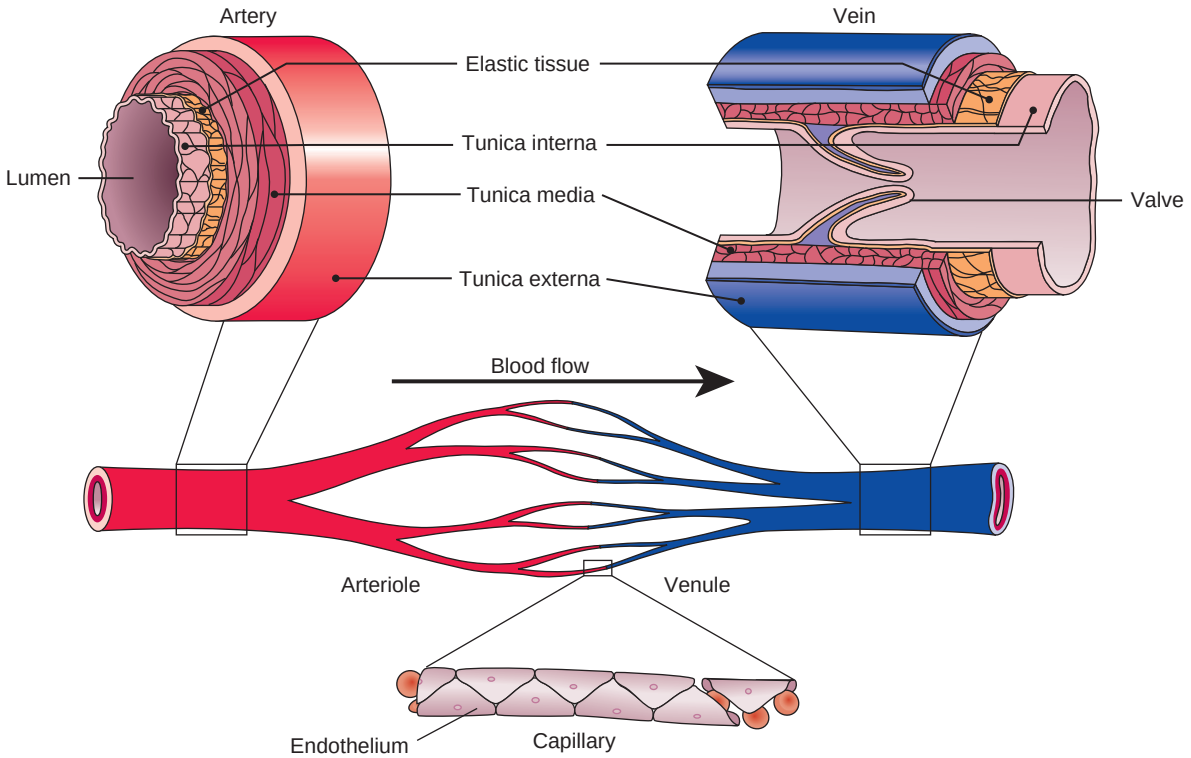

FIGURE 8.2. Anatomy of capillaries, veins, and arteries. (From Cohen BJ, Wood DL. Memmler's the human body in health and disease. 9th ed. Baltimore: Lippincott Williams & Wilkins, 1999.)

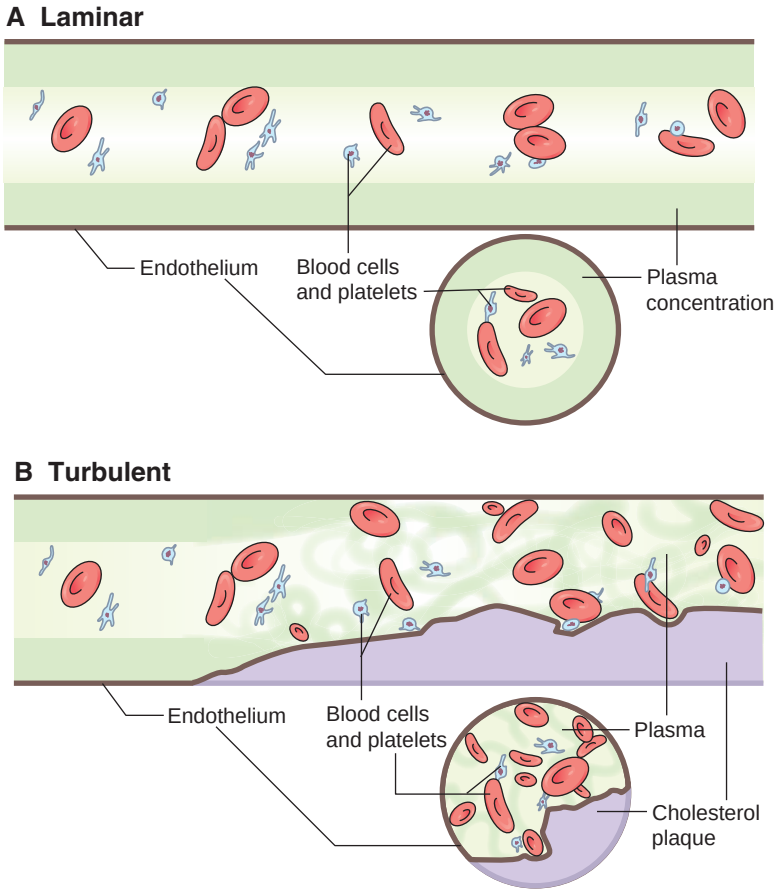

FIGURE 8.3. Laminar versus turbulent blood flow. **A.** Laminar flow. In laminar flow, the plasma is concentrated around the periphery of the vessel, allowing the solid blood components to flow through the center of the vessel. This maximizes flow rate and minimizes the chances for platelets and other solid components to initiate clot formation. **B.** Turbulent flow. Rough cholesterol plaques have formed within the interna of this vessel, causing the plasma to be deflected from the periphery of the vessel. When this occurs, the blood cells and other solid components of the blood are bounced off the endothelial walls, and the smooth flow of blood is interrupted. Clot formation is enhanced when platelets and other clotting factors come in contact with endothelial cells.

modified by the individual. Infrequently, high cholesterol may be associated with an autosomal dominant disorder called familial hypercholesterolemia that interferes with the removal or transportation of cholesterol out of the blood, resulting in markedly elevated blood cholesterol levels and a corresponding increase in the individual's risk for atherosclerosis. Diabetes mellitus is also a risk factor for atherosclerosis. While type 1 diabetes cannot be prevented at this time, type 2 diabetes can be prevented or its severity lessened in most cases by maintaining a healthy weight, staying active, and following a healthy diet. Interestingly, current research suggests at least an association between oral infections and the formation of atherosclerotic plaques; so periodontal infections may play a role in the development and progression of atherosclerosis. Refer to Application 8.1 for a discussion of this information.

Method of Transmission: Atherosclerosis is not transmissible. However, several risk factors for it including hypertension, type 2 diabetes, and hypercholesterolemia have a strong genetic base.

Epidemiology: Atherosclerosis is found more often in men than in women and is usually diagnosed between the ages of 40 and 70 (Ladich & Virmani, 2010). It is difficult to determine the number of people affected by this disease because most of the morbidity and mortality statistics are associated with coronary heart disease (CHD), stroke, heart attack, aneurysm, and peripheral vascular disease, all of which are major sequelae, or complications, of atherosclerosis. Some 75% of all deaths from cardiovascular diseases are ultimately caused by atherosclerosis (Roger et al., 2011).

Pathogenesis: Atherosclerotic lesions do not form on the inside of arteries but within the tunica interna. The exact mechanism behind the development of the lesions is not known. The lesions or plaques contain inflammatory cells, smooth muscle cells, lipids (mostly cholesterol), and connective tissues. They start out as flat or slightly elevated

APPLICATION **8.1**

The Oral–Systemic Link: What's the Connection?

The oral–systemic connection has been the topic of much research lately, and oral health has been shown to be an important aspect of total health. A recent analysis of available studies found a moderate positive association between periodontal infections and cardiovascular outcomes (coronary heart disease [CHD] and stroke). In addition, these findings suggest that periodontal infection is an independent contributor to the development and progression of atherosclerotic vascular diseases such as CHD and ischemic stroke (Kebschull et al., 2010). Four theories have been proposed to explain the link between periodontal infections and atherosclerotic disease. (For more information, refer to *Periodontal Disease and Overall Health: A Clinician's Guide* listed in the Media Menu at the end of this chapter.) In 2009, the American Academy of Periodontology and the American College of Cardiology published an Editor's Consensus Report in their respective journals, outlining clinical recommendations for treating patients with periodontitis and patients with atherosclerotic cardiovascular diseases (ACD). A brief outline of these recommendations follows:
(Friedewald et al., 2009; Genco Williams, 2010.)

- Patients with periodontitis should be told they may be at a higher risk for ACD. If they have one or more additional risk factors, for example, smoking or obesity among others, they should receive an explicit referral for a medical evaluation if they have not been evaluated within the last 12 months.
- Patients with periodontitis and cardiovascular risk factors should receive treatment to decrease these risks. The physician and dentist should comanage the patient's care, with the dentist playing a significant role in tobacco cessation, diabetes control, diet modification and weight control, and compliance with blood pressure medication regimens.
- Patients with ACD who do not have a diagnosis of periodontitis should be referred to a dentist for evaluation of the periodontium. If signs of periodontal infection are noted, periodontal therapy and maintenance should be instituted and the patients should be informed of the importance of managing their disease to decrease the effect of inflammation.
- Patients with both ACD and periodontitis should have members of both medical and dental teams working closely to reduce their risk factors, especially diabetes, smoking, and obesity.

The dental hygienist is in a very good position to take on the responsibility for carrying out a portion of these recommendations in collaboration with both the dentist and the physician. We possess the skills needed to help patients choose to make changes. Our experience with tobacco cessation strategies, several forms of risk assessment and management, and patient education from basic oral hygiene self-care to training patients to do oral self-examinations and more will enable us to take on this additional responsibility. Dental hygienists have the legal and ethical obligation to inform the patient of our findings relative to the signs of periodontal infection, such as bleeding, the cardinal signs of inflammation (redness, edema, etc.), increased probed pocket depths, and radiographic evidence of bone loss. These findings should be discussed with the dentist and the patient, and a plan of action including the potential need for referral for a medical evaluation should be developed and implemented. I believe this is an exciting opportunity for all involved, and while research is still being done and there are no definitive answers as yet, we should embrace the chance to expand our practice horizons while assisting our patients in attaining a healthy future.

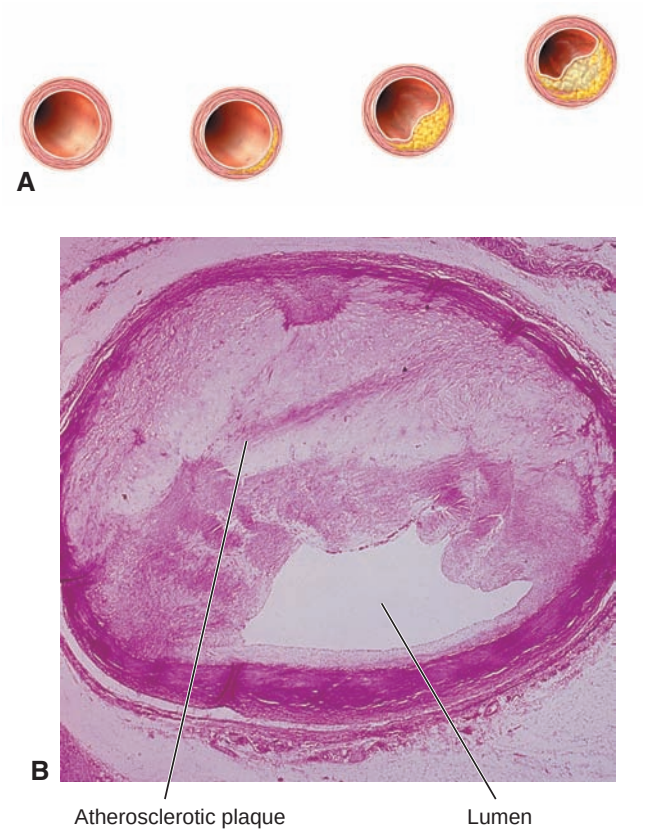

FIGURE 8.4. Atherosclerosis. **A.** Illustration showing the formation of atherosclerotic plaques. (Asset provided by Anatomical Chart Co.) **B.** Cross section of the renal artery showing significant narrowing of the lumen by atherosclerosis.

fatty streaks in the interna. As the disease progresses, the accumulation of cells and lipids increases, and the interna layer gets thicker, bulging into the artery and decreasing the diameter of the lumen (Fig. 8.4). As the lesions get progressively thicker, they change the geography of the inner vessel from slick and smooth to rough and bumpy. Blood pressure also changes because of atherosclerosis, since it takes more pressure to force blood through the narrowed areas. These changes cause the blood flow to become turbulent, resulting in an increased risk of both creating clots, injuring the inner lining (endothelium) of the vessel, or rupturing an atherosclerotic plaque. Injured endothelial surfaces increase the chance of thrombus formation because they are rough, and the substances the injured cells secrete attract blood products that encourage clot formation (see Chapter 9). Ruptured plaques expose blood to the contents of the plaque, most of which also encourage the formation of clots. Most often, a thrombus causes blockage of the artery and necrosis or **infarction** of the area supplied by blood from that vessel. Continued injury can weaken the walls of the vessel and lead to **aneurysm,** or a bulging and thinning of the vessel wall, and eventually to rupture of the artery.

Extraoral Characteristics: Clinical manifestations of atherosclerosis are only seen as they relate to the major complications or sequelae of the disease, which are discussed throughout this chapter. Infrequently, the hygienist may observe cutaneous lesions associated with high cholesterol levels called xanthomas. There are several types of xanthoma ranging from soft yellow-colored plaques found on the eyelid (Fig. 8.5) and under the eye to hard nodules found in the area of tendons (knees, elbows, knuckles). If the lesions are related to high cholesterol levels, they usually respond well to cholesterol-lowering medications, with most improving and about 50% resolving completely (Fair, 2009).

FIGURE 8.5. Xanthelasma. Yellowish plaque located on the upper eyelid toward the inner canthus is characteristic of this type of xanthoma. The patient reported higher than normal cholesterol but was not taking medication to control it.

Perioral and Intraoral Characteristics: Not applicable

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: Atherosclerosis is considered a contributing or etiologic factor for many of the cardiac and vascular disorders discussed in this chapter. Medications used to treat hypercholesterolemia may have dental implications ranging from xerostomia to adverse drug interactions. In addition, patients who have xanthomas and who have not had their cholesterol levels checked by a physician recently should be referred to their physician for evaluation.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment focuses on two areas: (1) eliminating or managing the risk factors and (2) managing the complications of the disease. Individuals at risk of, or affected by, atherosclerosis must make critical choices that will ultimately determine the length and quality of their lives. Risky behaviors such as smoking and physical inactivity need to be addressed and altered. Dietary changes lowering blood pressure, cholesterol, and lipid levels and those that help to prevent or manage type 2 diabetes are very important in reducing not only the risk of atherosclerosis but in decreasing the risk of complications from the disease. Maintaining tight glycemic control over both types of diabetes has been shown to decrease all of its complications including atherosclerosis. Medications can be used to assist

the individual in achieving lower blood pressure and lipid and cholesterol levels if dietary changes alone are not sufficient. The prognosis for atherosclerosis is determined by the complications the individual presents with. Treatment focusing on managing the complications of atherosclerosis as well as the prognosis of each condition is discussed as the complications are described in this chapter.

NAME: Hypertension

Etiology: There are two forms of hypertension: primary, also called essential, and secondary. Secondary hypertension is a sequela or consequence of another disease process such as renal disease or hyperthyroidism and will be eliminated if the disease causing it is eliminated or adequately treated. This section focuses on primary hypertension because 95% or more of cases of hypertension are considered primary. Primary hypertension has a multifactorial etiology that includes numerous genetic and environmental factors. Research has shown multiple genes are involved in determining a predisposition to hypertension. The exact genetic mechanism that triggers hypertension is unknown, as is the exact impact environmental factors have on the establishment and progression of the disease. However, we know atherosclerosis and type 2 diabetes have strong genetic tendencies and both are strongly associated with the development and progression of hypertension. Environmental risk factors associated with hypertension include smoking, high cholesterol and high salt intake, physical inactivity, and being overweight. Increasing age, being a male, and/or being of African descent are also considered risk factors.

Method of Transmission: Evidence points to a certain amount of genetic predisposition to hypertension, but the inheritance pattern is not understood and appears to be very complex. Otherwise, hypertension is a nontransmissible disease.

Epidemiology: The statistics related to hypertension are ominous; one of every three adult Americans is hypertensive. Overall, 39% of the population is normotensive or normal, 31% is prehypertensive, and 29% is hypertensive. Approximately 28% of those with hypertension are unaware of it (Chobanian, 2009). More men than women are hypertensive until the age of 55, when the trend reverses, and more women are hypertensive than men. Individuals of African descent have a much higher rate of hypertension than whites. In addition, hypertension in individuals of African descent is more severe and begins at an earlier age (Roger et al., 2011).

Pathogenesis: No matter what the etiology happens to be for an individual, the pathogenesis or development of primary hypertension involves at least one of the following: the kidney, sympathetic nervous system, and the blood vessels. The kidney controls blood volume by regulating salt and water balance with hormones such as aldosterone that affect vascular muscle tone and regulate renal blood flow and salt metabolism. The sympathetic nervous system stimulates vessels to contract or to dilate. Any change in the delicate balance between these systems can result in hypertension. Atherosclerosis, if present, narrows the lumen of blood vessels, increasing the amount of pressure needed to force blood through them. It also interferes with the ability of the vessel to dilate and lower blood pressure.

The major problem associated with hypertension is not the high blood pressure itself, but the effect high blood pressure has on almost every system in the body. Hypertension is a risk factor for the development of almost all cardiovascular diseases and disorders, kidney disease, stroke, and thrombohemolytic disorders. Prehypertension is recognized as a predictor of progression to stage 1 hypertension and studies have shown early forms of vascular damage in all of the organs affected by hypertension, such as the kidney. In addition, prehypertension is linked to type 2 diabetes and poor cognitive performance (Erdogan et al., 2007). Table 8.1 lists blood pressure categories and follow-up recommendations for medical referral suggested by the *Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.*

Extraoral Characteristics: Hypertension is usually asymptomatic. However, severe hypertension has been associated with headache, dizziness, **epistaxis** (nose bleeds), and visual disturbances.

TABLE 8.1 **Classification of Blood Pressure Measurements for Adults over 18 Years of Age**

	Blood Pressure Range			
Stage	**Systolic (mm Hg)**		**Diastolic (mm Hg)**	**Follow-Up Recommendation[a,b]**
Normal	<120	and	<80	Recheck in 2 years
Prehypertension[c]	120–139	and	80–89	Recheck in 1 year
Hypertension[c]	140–159	or	90–99	Recheck in 2 months
Stage 1	>160	or	>100	Refer for evaluation within 1 month
Stage 2	>180	or	>110	Refer for immediate evaluation

[a] If systolic and diastolic categories differ, follow recommendations for shorter time follow-up (e.g., 160/86 mm Hg should be evaluated or referred to source of care within 1 month).
[b] Modify the scheduling of follow-up according to reliable information about past BP measurements, other cardiovascular risk factors, or target organ disease.
[c] The classification is based on the average of two or more properly measured, seated BP readings on each of two or more office visits.
Adapted from Chobanian AV, et al. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension, December 2003;42:1206–1252, Tables 3 and 4, with permission.

APPLICATION **8.2**

Prehypertension: What's the big deal?

Most dental offices are now routinely obtaining their patient's vital signs, and, in fact, documentation of vital signs in the patient record is required by many state dental practice acts. But what are we doing with the information? It is easy to tell someone you found stage 1 or 2 hypertension and they really need to go to their physician for an evaluation, but what do you tell your patients when their blood pressure falls into that "fuzzy" zone called prehypertension? I hear the students in the clinic telling their patients "Your blood pressure is a little high today" or "You have prehypertension, but it is still not considered high blood pressure, so it is OK." Research is providing more and stronger evidence that prehypertension is not something to be fooled around with. We know it is a predictor of progression to hypertension and we are seeing more evidence everyday that even slightly high blood pressure over time can cause damage to the vessels in some of our most important organs like the heart and the kidneys (Chobanian, 2006). One of the reasons we take vital signs is to screen patients for hypertension; why then are we ignoring the opportunity to help our patients prevent hypertension by dealing with prehypertension? A simple discussion of what prehypertension means might be all that is necessary. Prehypertension means the person is at an increased risk of hypertension and in fact may already be experiencing damage to important organs affected by high blood pressure. We can discuss tobacco cessation, eating healthy, and getting more exercise, all of which will not only help prevent hypertension but will also help maintain a healthy oral environment. We should take prehypertension out of the "fuzzy" zone and address it with as much passion as we do periodontal disease and caries.

Perioral and Intraoral Characteristics: Not applicable

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: Each practice should establish guidelines for when to refer patients for medical evaluation and when to postpone dental procedures, based on current evidence (Table 8.1). Vital signs should be obtained at every dental appointment for every patient and dental professionals should inform their patients of the findings (see Application 8.2). Stress reduction protocols should be considered for all dental patients, especially for those with cardiovascular problems, including high blood pressure. Elective dental care should be postponed and a medical release obtained if the patient's systolic blood pressure is 180 or more and/or the diastolic pressure is 110 or more (Pickett & Gurenlian, 2010). When a patient's blood pressure is at these high levels, emergency dental care only should be performed and only performed in facilities that have access to emergency equipment and the appropriate personnel who would be needed in an emergency situation. In addition, dental professionals must be aware of the side effects of medications the patient is taking to control hypertension. Most will cause xerostomia, and protocols to prevent caries should be started as soon as possible. Most of these medications also cause orthostatic hypotension (decrease in blood pressure upon rising from a supine position) and measures to prevent this, such as keeping the patient in the chair for a few minutes prior to dismissal, are appropriate. The use of local anesthetics containing epinephrine (1:100,000) should be limited or avoided if possible because of their potential to increase blood pressure.

Differential Diagnosis: Not applicable

Treatment and Prognosis: The blood pressure treatment goal for patients who do not have diabetes is less than 140/90. If the patient has diabetes in addition to hypertension, the treatment goal is less than 130/80 (American Diabetes Association, 2011). The lower treatment goal for those with diabetes is based on the reported association between diabetes and an increase in the incidence of all forms of cardiovascular diseases, stroke, renal disease, and blindness (Chobanian et al., 2003). Blood pressure can be reduced by pharmacologic means and by changes in behaviors and/or lifestyles. The drugs most often prescribed regulate heart rate, decrease cardiac output, reduce vasoconstriction, and reduce levels of substances that would act to increase blood pressure, such as aldosterone and angiotensin. Diuretics have been returned to most basic treatment regimens because of their ability to lower blood volume initially and eventually to decrease peripheral resistance throughout the vascular system. Behavioral and lifestyle changes include losing weight; limiting alcohol consumption; decreasing sodium, saturated fat, and cholesterol intake; increasing aerobic activity; smoking cessation; and maintaining adequate dietary levels of potassium, calcium, and magnesium (Chobanian et al., 2003). The prognosis for those with hypertension obviously varies greatly with each individual, but when considered as part of a group, hypertensive individuals will become more hypertensive as they age. Untreated hypertension increases an individual's risk for early death.

Hypertensive Heart Disease

Hypertensive heart disease is caused by chronic hypertension and is characterized by hypertrophy of the left ventricle due to the heart working much harder than normal to pump blood through arteries and veins that have become narrowed by atherosclerosis or hardened by the persistent vascular trauma associated with hypertension. See Chapter 2, Figure 2.4 for an example of left ventricular hypertrophy due to hypertensive heart disease. Eventually, the heart can no longer compensate for the added work, and begins to

fail. Congestive heart failure (CHF) is the most common cause of death in hypertensive individuals who have not received treatment (Rubin et al., 2008).

NAME: Coronary heart disease (CHD)

Etiology: CHD occurs when the oxygen demands of the heart muscle are not met because blood flow to the heart muscle through the coronary arteries is inadequate. The most common cause of CHD is atherosclerosis. Anything that causes development of atherosclerosis will contribute to the risk of developing CHD. High cholesterol, poor dietary habits, inactive lifestyles, smoking, diabetes, hypertension, age, and genetics all play a role in determining an individual's risk of developing atherosclerosis and, subsequently, CHD.

Method of Transmission: CHD is not passed from person to person; however, a family history of CHD can sometimes be linked to a genetic abnormality called familial hypercholesterolemia.

Epidemiology: Approximately every 25 seconds, an American will experience a coronary event, and approximately every minute, someone will die of one (Roger et al., 2011). CHD is the number one killer of Americans. In 2008, 16,300,000 Americans, or 7% of the population, had CHD (Roger et al., 2011).

Pathogenesis: There are two basic types of CHD: chronic ischemic heart disease and acute coronary syndromes. Chronic ischemic heart disease includes stable angina and silent myocardial ischemia and occurs when the blood supplied to the heart by the coronary arteries is not adequate to meet the demands of the heart muscle. This does not normally occur until one or more of the coronary vessels are 75% or more occluded. Usually, the ischemia is not noticeable until the heart is exposed to stress that increases the heart rate, such as physical exercise (shoveling snow), emotional stress, cold temperatures, and large meals. The normal blood flow through the obstructed arteries is not sufficient to supply the needs of the heart muscle when stressed, and ischemia occurs. Ischemia can cause symptoms as it does in **angina,** or angina pectoris, or no symptoms as in silent myocardial ischemia. The reason for silent myocardial ischemia is not clearly understood and it is not known how many people suffer from this form of CHD. Individuals with diabetes have the silent form more often than the symptomatic form. In this case, the lack of pain may be the result of impaired sensory nerve transmission within the autonomic system, or **autonomic neuropathy** (see Chapter 7).

Acute coronary syndromes include unstable angina, myocardial infarction (MI), and sudden death. **Unstable angina** describes an increase of the symptoms of angina usually ending in a myocardial infarction. Angina pain occurring during rest is the most common sign of progression to unstable angina. MI causes the actual death of myocardial cells due to a prolonged lack of oxygen. The severity of the infarction depends on the amount of heart tissue affected, the location of the infarct, and the length of time the heart cells are without oxygen. If blood flow is restored to the affected area within 15 to 20 minutes and the heart muscle cells begin to function correctly, permanent damage may be avoided. If the cells do not function correctly, a condition known as **ventricular fibrillation** (heart quivers but does not produce a functional beat) may occur and outside intervention in the form of defibrillation may be the only way to save the person's life. The ventricular fibrillation, in these cases, may be the actual cause of death rather than the damage done to the heart cells. If blood flow is not restored, the myocardial cells undergo necrosis and fibrous scar formation. Scar formation takes between 6 and 8 weeks and leaves the heart muscle compromised because the scar tissue will not function like cardiac muscle. How badly the heart is compromised depends on the number and location of the cells destroyed. Sudden death is also considered an element of acute coronary syndromes. When an individual dies within 1 hour of the onset of symptoms of a myocardial infarction, it is called sudden death. Sudden death is most often associated with severe dysrhythmia, usually ventricular fibrillation.

Extraoral Characteristics: Angina pain usually centers in the substernal area of the chest and is described as crushing, suffocating, or "like having an elephant stand on your chest." The pain is normally severe enough to stop the individual from doing whatever he or she is doing. The pain may stay in the chest area or may radiate up into the left jaw or into the left arm; the right arm may also be affected. If the pain is not severe, chest pain can be easily confused with indigestion or the arm and shoulder pain with arthritis. Symptoms associated with an acute myocardial infarction are varied, and many people who have had myocardial infarctions are not aware they have had them. In fact, 25 to 50% of nonfatal myocardial infarctions are not symptomatic and are identified only later by electrocardiogram or at autopsy (Rubin et al., 2008). Whether the pain is severe or not, the patient may also present with nausea, vomiting, shortness of breath, and copious sweating, or the patient may only experience one or two symptoms or a lesser degree of all of the symptoms.

Perioral and Intraoral Characteristics: Not applicable

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: The dental health care provider should consult with the patient's cardiologist in order to determine the appropriate time to initiate dental treatment after an acute MI. Prior to 2007 the American College of Cardiology and the American Heart Association advised postponing elective dental care for 3 to 6 months after an MI. In 2007 this was revised to 30 days with the recommendation that health care providers consult with the cardiovascular physician to determine the patient's status and risk for adverse cardiovascular events (Fleisher et al., 2007; Pickett, 2011). No dental care should be rendered to someone with unstable angina except in a setting where appropriate life support is immediately available. Stress

BOX 8.1

Dental Implications of Antithrombotic Therapy

Even though antithrombotic therapy is very common, there is still uncertainty among many dental and medical health care practitioners as to how to manage these patients (See Clinical Protocol #21 for more information). Practitioners may still believe they must interrupt antithrombotic therapy prior to invasive procedures such as tooth extraction or even nonsurgical periodontal debridement. It is not appropriate to stop or interrupt therapy without consulting the prescribing physician. Data indicate that interrupting or reducing antithrombotic therapy prior to dental surgery may not only be unnecessary but may actually cause the formation of thrombi resulting in death of the patient (Hirsh et al., 2003; Jaffer, 2009; Napenas et al., 2009; Grimes et al., 2007). Suggested management strategies include establishing the reason for antithrombotic therapy and determining the patient's coagulation status prior to dental treatment during which bleeding is anticipated. A medical consultation may also be indicated to make sure all necessary information about the patient is known by the dental health care workers. In cases where the INR is too high (<5.0) for the patient to safely undergo a specific procedure, there are protocols which the physician can employ to lower the INR without endangering the patient, but it must be done under the auspices of the prescribing physician. Patients on low-dose anticoagulant therapy (including aspirin) do not have a high risk of major blood loss during routine dental procedures (Jeske & Suchko, 2003). However, it remains a good policy to consult with the physician and determine the current clotting status of the individual also.

All clinicians should be familiar with local measures to control bleeding such as direct pressure (biting on a moistened tea bag containing tannic acid, a hemostatic agent), tranexamic acid or epsilon aminocaproic acid (EACA) rinses, gelatin sponges, suturing, and using atraumatic surgical techniques (Jeske & Suchko, 2003).

Several medications commonly prescribed in dentistry can interfere with clot formation and should be avoided when treating a patient on antithrombotic medication. The following medications are contraindicated for patients on antithrombotic therapy.

Increase Prothrombin Time (Decrease Clot Formation)

- Aspirin
- Other nonsteroidal anti-inflammatory medications
- Tetracycline
- Erythromycin
- Clarithromycin
- Metronidazole

Decrease Prothrombin Time (Increase Risk of Clot Formation)

- Penicillins

reduction techniques should be used to limit anxiety during dental appointments, and supplemental oxygen should be considered if appropriate. Drugs used to manage CHD have many oral side effects, and the professional should be aware of the specific side effects associated with each type of drug. For example, calcium channel blockers are associated with gingival hyperplasia. When gingival hyperplasia is identified, the dental professional may consult with the patient and the patient's physician to develop a plan to try to prevent any further hyperplastic growth. Each patient should be evaluated for the presence of xerostomia because many of the drugs prescribed for CHD will cause xerostomia. Patients may also be on an antithrombotic treatment regimen. Antithrombotic therapy is prescribed for many different conditions discussed in this and other chapters; therefore, the dental implications associated with this therapy are presented in Box 8.1 and may be referred back to as necessary. Additional information may be found in Clinical Protocol #21. A consultation with the physician may be required to determine the coagulation status of the patient. The most common test to determine a patient's coagulation status is prothrombin time (PT); please refer to Box 8.2 for information on this test and the international normalized ratio (INR) used to standardize the results of the PT. Above all, each patient should be encouraged to maintain as healthy an oral environment as possible to limit the systemic effects of oral infections. As always, each dental professional should be able to recognize the signs and symptoms of a cardiac emergency and be trained to use cardiopulmonary resuscitation (CPR) and the automated external defibrillator (AED) if an emergency occurs.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment for CHD depends on the specific type of disease present. Treatment for chronic ischemic heart disease focuses on relieving symptoms and preventing acute coronary syndromes. Current treatment is aggressive and aimed at not only medical and surgical therapies but also on eliminating preventable risk factors such as smoking and managing disorders that are associated with progression of this disease such as hypertension, diabetes, and high cholesterol. Medications such as

BOX 8.2

Coagulation Status: What Do the Numbers Mean?

Prothrombin time (PT) is the most relied upon test for coagulation status; normal PT time is between 10 and 13 seconds. Individuals taking anticoagulant medications will have results that are 1.5 to 2.0 times normal or between 15 and 32.5 seconds. However, there is a problem with consistency of the results of this test, which historically varied between laboratories and materials or reagents used, setting the stage for inaccurate interpretation of the results. The international normalized ratio or INR was developed to correct these differences mathematically, creating a standardized measure of clotting time expressed in values from 1.0 to 10.0 and more, with 1.0 defined as normal. The target INR for most anticoagulant therapy regimens falls between 2.5 and 3.5. Studies have shown that routine dental procedures including uncomplicated surgery may be done safely at an INR between 1.0 and 4.0, provided local hemostatic measures are used and there are no other contraindications (Jeske & Suchko, 2003). INR levels between 4.0 and 5.0 may require alteration of the patient's anticoagulation medications, which should be done only by the prescribing physician. Levels over 5.0 are a contraindication to any invasive procedures (Jeske & Suchko, 2003).

nitroglycerin are used to treat the symptoms of angina by relaxing systemic blood vessels and thereby decreasing cardiac workload and lessening the oxygen requirements of the heart muscle. Drugs that decrease the heart rate and decrease cholesterol levels are considered life prolonging and are a mainstay of therapy for CHD, as are medications that reduce the potential for thrombus formation in atherosclerotic arteries, specifically antithrombotic (anticoagulant and antiplatelet) agents. Surgical treatment is often necessary to reestablish adequate blood flow to the heart muscle. These interventions include coronary angioplasty, the placing of stents or wire tubes that hold the arteries open, and coronary artery bypass procedures. In coronary angioplasty, a collapsed balloon is threaded through arteries in the groin to the coronary artery that is blocked. The balloon is placed in the narrowed area and then inflated, causing the matter within the interna and in the lumen of the vessel to be compressed resulting in a larger lumen. A stent may be placed in the artery to maintain the open position (Fig. 8.6). Coronary bypass surgery uses a vein graft from the leg to go around, or bypass, a blockage in one or more of the coronary arteries, thus reestablishing blood flow to the area.

Treatment of acute coronary syndromes focuses on reestablishing blood flow to the area of infarction as soon as possible to limit the extent of permanent damage, ideally within 60 to 90 minutes of the onset of symptoms. Drugs that dissolve blood clots, or thrombolytic drugs, are known to reduce the incidence of death and limit the extent of damage. Aspirin is a strong antiplatelet drug that can be given to someone who is experiencing a myocardial infarction, even before medical help is obtained. Aspirin has been shown to increase survival chances by decreasing the chance of new or larger clot formation. Definitive therapy for acute coronary syndromes is basically the same as for chronic ischemic heart disease, only performed under emergency conditions.

Individuals who have had experience with these diseases should take part in a cardiac rehabilitation program designed specifically to meet their needs. The rehabilitation programs are meant to safely return a person with CHD to as normal a routine as possible and to address changes that need to be made such as diet and tobacco use.

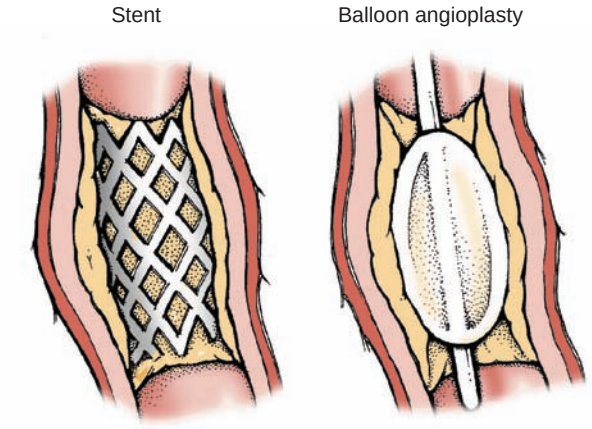

FIGURE 8.6. Balloon angioplasty. Atherosclerosis treatment. Close-up views of coronary arteries showing balloon angiography and stent placement, both of which are intended to increase blood flow to the heart. (Image courtesy of LifeART, Lippincott Williams & Wilkins. All rights reserved.)

Peripheral Artery Disease

Peripheral artery disease (PAD) is atherosclerosis involving the arteries of the lower extremities. As with coronary artery disease, it involves a progressive narrowing of the lumen due to atherosclerotic plaque development within the interna. The risk factors for PAD are almost identical to those for atherosclerosis, with smoking cigarettes and a history of diabetes mellitus heading the list. In fact, more than 80% of those with PAD are current or former smokers (Porth, 2011). The narrowed vessels cause ischemia in the area they supply when increased demand is placed on them to provide more oxygen as in the case of exercise such as walking. The most common symptom is calf pain when the person walks; other symptoms include a vague aching or slight numbness in the leg and/or foot. Clinically observable signs such as thinning of the skin, brittle toenails, hair loss, atrophy of the muscles, cool to the touch skin, and weak pulses in the leg and foot will occur as the disease progresses. In the final stages, the vessels are so narrowed they do not provide enough oxygen to keep the cells functioning in an area. Ulceration of the skin surface will lead to more tissue necrosis and eventually gangrene.

Treatment revolves around eliminating risk factors such as smoking, getting the individual up and walking, controlling diabetes, and providing appropriate medications such as antithrombotics and vasodilators. In severe cases, surgical intervention to bypass the affected artery or place a stent to open the artery is necessary.

Dental implications of PAD include those associated with the coagulation status of the individual and the side effects of medications, and patient education and support for tobacco cessation and control of diabetes. The patient should be evaluated for periodontal disorders, and, if present, the oral-systemic connection between periodontal infections and atherosclerotic disease should be discussed. In addition, the dental hygienist may be able to identify an individual at risk for this condition during the review of the health history and vital signs and provide a referral for a medical evaluation.

NAME: Abdominal aortic aneurysm (AAA)

Etiology: Aneurysms are localized weaknesses that result in bulges or bubbles in the wall of an artery. AAA is an aneurysm located in the abdominal aorta. Most AAAs are caused by atherosclerosis and related hypertension; they can also be caused by congenital defects, trauma, or infection. Smoking is strongly associated with both atherosclerosis and AAA (Pearce & Annambhotla, 2012).

Method of Transmission: Genetic influences appear to play a part in the development of AAA. The tendency to form AAA is a component of many inherited connective tissue disorders,

such as Marfan and Ehlers-Danlos syndromes. AAA caused by an infectious process is associated with syphilis, tuberculosis, and, more often, infective endocarditis. Preventing and treating these infections would effectively eliminate the chance of transmitting the responsible organisms.

Epidemiology: Ruptured AAA is the 13th leading cause of death in the United States. (Pearce & Annambhotla, 2012). Most of these cases will be asymptomatic and diagnosed at autopsy. AAA is uncommon in those of African descent, Asians, and Hispanics. It is more common in men than in women and probably starts developing at age 50, with a peak incidence in men at age 80.

Pathogenesis: The pathogenesis of an AAA is essentially the same regardless of the actual cause. Most AAAs are located just below where the renal arteries branch off the aorta and prior to the bifurcation of the aorta into the iliac arteries, but they can affect any or all of these arteries (Fig. 8.7). Once the vessel wall is weakened, it begins to expand under the constant pressure from blood being forcefully pumped through it. As the aneurysm expands, there is increased risk of thrombus formation or, more commonly, rupture of the vessel.

Extraoral Characteristics: Most AAAs are asymptomatic and are often found by mistake when looking for something else. As the aneurysm enlarges, there may be pain focused in the lower back or in the groin area and the individual may experience dysphagia (difficulty swallowing). A pulsating mass in the belly around the area of the umbilicus may be observed. A thrombus that forms in the aneurysm may become detached from the vessel wall and move through the circulation with the flow of blood. When this occurs, the blood clot is known as an **embolus.** An embolus may lodge in another area, blocking the flow of blood, causing **ischemia** (lack of oxygen) in that area.

Perioral and Intraoral Characteristics: Not applicable

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: Patients diagnosed with an abdominal aneurysm may be taking medications such as beta-blockers to lower blood pressure and help prevent enlargement of the aneurysm. Xerostomia is often a side effect of this type of medication and will need to be managed. In addition, identification of an individual who is at risk and knowledge of the warning signs, such as back pain or dysphagia, may prompt a medical referral that could save a life.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Since atherosclerosis is associated with many AAAs, much of the medical treatment focuses on reducing the risk factors associated with progression of the atherosclerosis. This includes managing hypertension, hypercholesterolemia, and diabetes. Small aneurysms are monitored for signs of progression, and large aneurysms, such as the one in Figure 8.7, need to be surgically corrected. The most common treatment is to replace the damaged part of the aorta with a synthetic Dacron graft. The renal and iliac arteries can be attached to this graft if necessary, depending on the extent of aortic involvement. The prognosis is very poor for an untreated or undiagnosed large AAA. AAAs of 4 cm or less have a 2% chance of rupture, and those over 5 cm have a 25 to 40% chance of rupture within 5 years after diagnosis. A ruptured AAA is a life-threatening emergency,

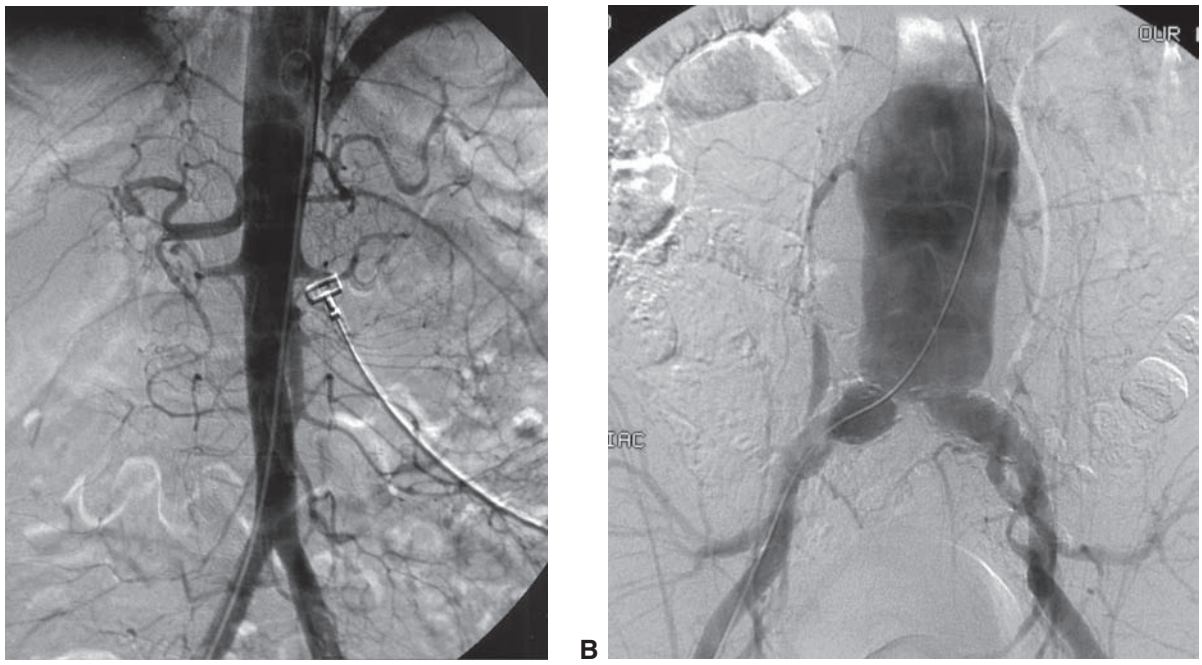

FIGURE 8.7. Abdominal aortic aneurysm. **A.** Normal aorta and iliac arteries. **B.** Abdominal aneurysm 8 cm in diameter affecting the aorta and the iliac arteries.

with over 50% causing immediate death from **exsanguination,** or bleeding out (Rubin et al., 2008).

NAME: Raynaud disease (primary) and Raynaud phenomenon (secondary)

Etiology: Raynaud disease appears to have no specific cause, while Raynaud phenomenon is associated with other diseases, including scleroderma and lupus erythematosus. Raynaud phenomenon is also linked to previous trauma such as frostbite or occupational trauma such as carpal tunnel syndrome and other repetitive stress disorders. Both forms share the same characteristics.

Method of Transmission: None

Epidemiology: Raynaud disease is estimated to be found in 5% of the population. There is no race predilection, but it appears more women are affected than men. It is usually diagnosed under the age of 30. (Narayanan et al., 2009). The incidence of Raynaud phenomenon is related to the incidence of the disease or trauma with which it is associated.

Pathogenesis: The symptoms of this disorder are caused by ischemia of the cells in the fingers, toes, and sometimes the ears and nose. The ischemia is the result of episodes of vasospasms in the small arteries of the skin brought on by cold and/or emotional stress. Raynaud disease has also been associated with smoking.

Extraoral Characteristics: The first sign of an episode is a color change in the affected tissues from normal to pale and then cyanotic (Fig. 8.8). The color change is accompanied by numbness and tingling. The end of an episode is characterized by increased redness, pain, throbbing, and altered sensations (Fig. 8.9). The fingertips are affected more often than the toes, nose, and ears.

Perioral and Intraoral Characteristics: Occasionally, the lips may be affected by this condition.

Distinguishing Characteristics: Numbness and color change in the fingers or other body part is characteristic of this disorder.

FIGURE 8.8. Raynaud disease or phenomenon. Characteristic pallor of the fingertips associated with vasospasms characteristic of Raynaud disease or phenomenon. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

FIGURE 8.9. Raynaud disease or phenomenon. Erythema associated with the end of an episode. This patient reports the erythema and altered sensations that used to resolve between episodes are now constant.

Significant Microscopic Features: Not applicable

Dental Implications: Many of the underlying causes of Raynaud phenomenon are very serious, such as forms of cancer, heavy metal toxicity, systemic lupus, rheumatoid arthritis, and scleroderma. Therefore, it would be appropriate to refer an individual complaining of these symptoms for a medical evaluation. Medications used to treat the disorder, such as calcium channel blockers, may have dental implications and the patient should be evaluated for any oral effects.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Most cases of Raynaud disease do not need treatment other than avoiding such precipitating factors as cold and stress and protecting the areas during an episode. The most severe cases may be treated with medications, such as calcium channel blockers, which support vasodilation, or a surgical procedure that cuts the sympathetic nerve supply to the area, thereby reducing the occurrence of vasospasms. In rare cases, severe disease can result in necrosis of the tips of the fingers or other affected tissues, which would then have to be surgically removed.

NAME: Thromboembolic venous disorders

Etiology: Although not completely understood, thrombus (blood clot) formation is known to be associated with endothelial injury (injury of the inner lining of the blood vessels), blood stasis or slow flow, and hypercoagulability.

Method of Transmission: Not applicable

Epidemiology: The American Heart Association estimates that 100 of every 100,000 persons in the United States will experience an initial venous thrombosis every year. Deep venous thrombosis (DVT) will account for two-thirds of this number, and pulmonary embolism (PE) will account for the other one-third. Men have a higher incidence of this disease than women, and the overall incidence increases with age. Whites and Blacks are more likely to experience venous thrombosis than Hispanics or Asians (Roger et al., 2011).

BOX 8.3

Factors Associated with the Development of Deep Venous Thrombosis

Stasis

- Heart failure
- Venous obstructions
- Immobility due to bed rest, paralysis, or inactivity
- Myocardial infarction

Hypercoagulation

- Oral contraceptive use
- Pregnancy
- Childbirth
- Stress
- Cancer

Vascular Trauma

- Severe accidental trauma
- Surgical trauma
- Severe infections

Pathogenesis: Box 8.3 lists risk factors associated with the development of venous thromboembolisms. Although thrombi can form in any area, the most common site is in the deep veins of the leg, where it is called DVT. When a thrombus breaks away from the endothelium and becomes an embolus, it can travel through the circulatory system and end up anywhere. Very often, emboli find their way into the pulmonary circulation and lodge in the lungs as PE.

Extraoral Characteristics: Individuals with DVT may be asymptomatic and may never have any complications from their disease. The symptoms associated with DVT are deep muscle pain and swelling in the area **distal** to the clot or away from the trunk. There is potential for fever, malaise, and other general signs of inflammation as well.

Symptoms associated with a PE are directly related to the size of the embolus and the health of the individual. A small PE may be asymptomatic or may cause dyspnea (difficult breathing) and tachypnea (fast breathing). A large PE may cause areas of necrosis and scarring in the lung, which will impair lung function. Large emboli may lodge in the bifurcation of the pulmonary artery and obstruct blood flow to both lungs, causing severe hypotension and sudden death. Smaller emboli that obstruct 50% or more of the lungs also have a high risk of causing death.

Perioral and Intraoral Characteristics: Not applicable

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: Individuals who have a thromboembolic venous disorder will be taking antithrombotic medications. A medical consultation to determine coagulation status is appropriate prior to dental procedures expected to cause bleeding. Sudden symptoms of difficult breathing or unconsciousness, which might indicate that a clot is obstructing vital circulation, should prompt the dental professional to activate emergency medical services (EMS).

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment for DVT consists of antithrombotic therapy to stop further thrombus enlargement or formation and fibrinolytic therapy to dissolve the thrombus. Surgery may be necessary to remove thrombi that are not responding to medical interventions or to place a filter into the vena cava to prevent emboli from the legs from entering the heart and going to the brain or lungs. Individuals who have had one episode of DVT are at very high risk of experiencing more. Prevention is a very important aspect of treatment for the individual at risk for DVT or who has already experienced DVT. Prevention focuses on antithrombotic therapy and using physical exercise (such as walking) and mechanical means (such as support stockings or air compression devices) to help move blood more quickly through the venous system in the lower extremities. Almost one-third of individuals with PE die from complications of the disease (CDC).

NAME: Stroke (cerebral vascular accident)

Etiology: A stroke is caused by partial or total obstruction of blood flow to the brain. There are two forms of stroke: cerebral ischemia (infarction) and intracranial hemorrhage. Cerebral ischemia is caused by occlusion of the cerebral arteries by a thrombus or an embolus. The most common causes of intracranial hemorrhage are trauma, hypertension, and aneurysm, specifically "berry" aneurysm. Berry aneurysms are small sac-like bulges in the bifurcations or junctions of vessels in the brain. The most common area for berry aneurysm formation is in the circle of Willis (Fig. 8.10).

Method of Transmission: Genetic predisposition associated with both atherosclerosis and hypertension plays a role in stroke occurrence. Otherwise, stroke is not a transmissible disorder.

Epidemiology: Approximately 795,000 new or recurrent strokes occur annually in the United States; essentially,

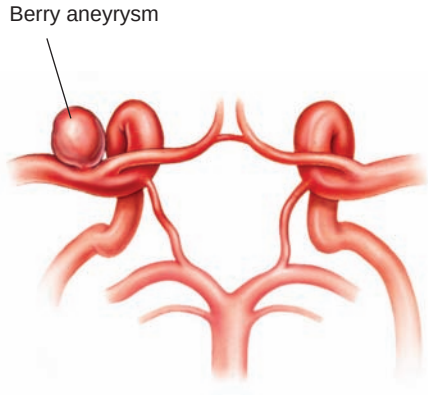

FIGURE 8.10. Berry aneurysm. The major blood vessels supplying the brain branch off the circle of Willis, located in the floor of the cranial cavity. The circle of Willis is a common area for the development of berry aneurysms. (Reprinted with permission from Porth CM. Pathophysiology. 6th ed. Philadelphia: Lippincott Williams & Wilkins, 2002.)

someone has a stroke every 40 seconds. The incidence of stroke is higher in women than men and is almost twice as high in individuals of African descent as in Whites. The incidence of stroke increases with age (Roger et al., 2011).

Pathogenesis: Ischemic-type strokes account for about 87% of all strokes (Roger et al., 2011). In ischemic stroke, blood flow is either gradually decreased by a growing thrombus or suddenly obstructed by an embolus. In either case, the brain cells located distal to the obstruction become necrotic. Typically, the lesion shows a central area of necrosis and a larger surrounding area that has the potential to recover. Initial emergency treatment of the ischemic stroke focuses on restoring blood flow to this larger surrounding area, thereby limiting the extent of the permanent damage.

Often, individuals who are at risk of ischemic strokes have a temporary obstruction of a cerebral artery, or a **transient ischemic attack (TIA),** that results in temporary neurologic signs and symptoms. There is overwhelming evidence these transient attacks are warning signs signifying a sharp increase in an individual's risk for a stroke, as 15 to 40% or more of strokes are preceded by TIAs (Roger et al., 2011; National Stroke Association, 2010).

Hemorrhagic strokes are less common than ischemic strokes but are more frequently fatal. Rupture of the blood vessels in the brain results in increased pressure in the brain causing interruption of blood flow and necrosis of tissues in the affected areas.

Extraoral Characteristics: Common symptoms of stroke include full or partial paralysis involving one side of the body, visual disturbances including double and blurred vision, inability to speak or slurred speech, dizziness, and a change in the level of consciousness. Hemorrhagic strokes may also present with nausea, vomiting, severe headache, loss of consciousness, and coma.

Perioral and Intraoral Characteristics: It is common for stroke symptoms and after effects (both permanent and temporary) to be observed in the oral area. Unilateral weakness may affect chewing, swallowing, and the ability to clear the mouth of residual food. The patient may appear to drool uncontrollably, not due to excessive salivation but to a decrease in the ability to swallow or to know when to swallow. Patients will favor chewing on the unaffected side of their mouths, so the natural cleansing mechanism of the oral cavity is impaired. Food pocketing is also a problem with some stroke patients because they cannot feel the location of the food, and it stays in the mucobuccal fold area and in other nooks and crannies within the oral cavity. There is usually at least some motor impairment that makes oral hygiene self-care quite difficult for many patients after a stroke.

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: The dental implications associated with stroke fall into four categories as follows:

1. Management of the side effects of medications taken to prevent thrombus formation (Box 8.1).
2. Management of poststroke physical effects. The severity of physical impairment ranges from insignificant to total incapacitation. The dental professional must evaluate the impact general physical as well as oral and perioral impairments have on the physical, mental, and oral health of the individual. Dysphagia, food pocketing, speech impediments, drooling, and other manifestations of neurologic damage can adversely affect all aspects of the person's well-being. Dental professionals will want to work in cooperation with other health care professionals to develop a plan maximizing the patient's recovery potential.
3. Home care modifications. The dental hygienist is the ideal person to evaluate the patient's ability to perform home care procedures. Home care modifications should be based on the individual's level of function. Every effort should be made to help the patient achieve as much autonomy as possible through modification of home care implements, such as toothbrushes, and practices, such as using supplemental fluorides. If the patient must have help from a caregiver, the dental hygienist should provide hands-on instruction to make oral health maintenance as effective and as easy as possible.
4. Emergency management of stroke. If the dental professional suspects a patient is having a stroke, EMS should be summoned immediately. Refer to Application 8.3. Aside from reassuring the patient and keeping him or her comfortable, little can be done in the dental office other than positioning the patient in an upright or semisupine position to limit blood flow to the brain, providing supplemental oxygen, and monitoring vital signs. The presenting symptoms may be vague, and the patient may not want to attend to them immediately. Therefore, the most important contribution the dental professional can make is to recognize the symptoms associated with stroke and act appropriately, even if in doubt, because time is of the essence. Quick administration of medical treatment may prevent extensive permanent damage.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment protocols for ischemic and hemorrhagic strokes differ. With ischemic strokes, the emphasis is to treat rapidly and to try to preserve as much brain tissue as possible. Thrombolytic drugs (also known as "clot busters") are highly effective but must be given within 3 (and under specific circumstances up to 4.5) hours of the onset of stroke symptoms or not at all (del Zoppo et al., 2009). These drugs are used to dissolve blood clots and reestablish circulation to the area of the brain that still has the potential to recover. Hemorrhagic strokes have no specific therapy except to monitor the patient and provide basic and advanced life support. Surgical removal of the intracranial

APPLICATION **8.3**

Stroke: Can you recognize the signs and symptoms?

Do you think you could recognize the signs and symptoms of a stroke if your patient were experiencing them? Would you be able to identify a possible TIA? If you said "no," you are not alone; few people outside of health care are aware of this information. Organizations and agencies involved with strokes such as the National Stroke Association, the Stroke Collaborative, and the American Stroke Association have been hard at work to increase the public's knowledge of the warning signs of a stroke, ultimately hoping to reduce deaths and permanent disability by getting patients to a treatment center as quickly as possible. They have developed public awareness campaigns using catchy mnemonics to help people remember the warning signs and what to do. For example, from the National Stroke Association:

FAST
F—Face: Ask the person to smile. Does one side of the face droop?
A—Arms: Ask the person to raise both arms. Does one arm drift downward?
S—Speech: Ask the person to repeat a simple sentence. Does the speech sound slurred or strange?
T—Time: If you observe any of these signs, it's time to call 911 or get to the nearest stroke center or hospital.

Other signs stressed by these campaigns include sudden numbness especially on one side of the body; sudden confusion, trouble speaking or understanding; sudden trouble seeing in one or both eyes; sudden trouble walking, dizziness, loss of balance or coordination; and sudden severe headache with no known cause. Waiting to get appropriate care is the enemy. Noting the time symptoms first occurred is extremely important in determining whether a specific thrombolytic (clot buster) medication, recombinant tissue plasminogen activator (rtPA), can be administered. If the patient gets to the hospital within 3 hours after the first symptoms of stroke and there are no other contraindications, this medication can be given. In specific circumstances, rtPA may be given up to 4.5 hours after the start of symptoms. This medication can mean the difference between a normal future and one with severe and permanent disabilities caused by the stroke. What is your responsibility? Make sure you can recognize these symptoms and don't be afraid to call 911. Discuss this information with your patients especially those at risk for stroke and their family members. Doing this just may save someone's life someday!

For more information, visit the National Stroke Association web site, available at: *http://www.stroke.org*.

hematoma may be successful in limiting the mortality and disability associated with hemorrhagic strokes.

Stroke is considered to be the third leading cause of death (heart disease and cancer are first and second) in the United States, with approximately one death occurring every 3 minutes. In addition, stroke is the leading cause of long-term disability, causing permanent disability in up to 30% of those affected (Roger et al., 2011).

Heart Disorders

Although the heart has a very romantic history, it is in reality a muscular pump with the capacity to work nonstop for the life of the individual, or approximately 70 to 80 years. When the heart stops pumping, life as we know it ceases. Many of the medical problems of dental patients involve the heart, and many of the procedures dental professionals perform have an impact on the heart. We must have a basic understanding of how the heart works and how diseases of the heart impair its function. This knowledge will enable us to recognize potential problems and modify planned treatment to protect the patient and provide the safest and most appropriate therapy possible.

In addition, the practitioner will be able to determine the appropriate education topics and select materials directed toward informing the patient about risks associated with poor oral health and motivating the patient to improve oral hygiene practices at home if necessary. For additional information, refer to Clinical Protocol #17 for more suggestions on management strategies related to caring for the patient with a cardiac disorder in the dental office environment.

Cardiac abnormalities include both congenital and acquired disorders affecting the form and function of the heart muscle, valves, blood supply, and conduction of electrical impulses. The following sections focus on these abnormalities.

NAME: Congenital heart defects

Etiology: The exact etiology of most congenital heart defects is not known. However, there is growing evidence that implicates a combination of genetic and environmental factors in the development of most congenital heart defects. Box 8.4 lists many of the known environmental causes of congenital heart defects. Many of the more common genetic syndromes include congenital heart defects; some of these syndromes are listed in Box 8.5. As the role of genes in the development of heart defects continues to be uncovered, there will be many opportunities to find ways to intervene and possibly prevent heart defects (MOD, 2011).

Method of Transmission: Congenital heart defects are not transmitted except in cases of maternal infections and through inheritance.

Epidemiology: The American Heart Association estimates 8 congenital heart defects occur per 1,000 live births in the United States annually (about 36,000 defects). Approximately 2.3 per 1,000 or 9,200 babies born with

BOX 8.4

Environmental Factors Associated with Congenital Heart Defects

Maternal Infections
- Rubella
- TORCH syndrome agents

Maternal Illness
- Diabetes
- Phenylketonuria (PKU)

Maternal Medications/Drugs
- Retinoids (Accutane)
- Lithium
- Alcohol
- Cocaine
- Cannabis
- Phenytoin
- Tobacco
- Dextroamphetamine
- Vitamin D
- Thalidomide
- Estrogenic steroids
- Higher maternal age
- Paternal cocaine use

these defects will need surgical intervention to correct or manage the defects. Males, females, and different ethnic groups seem to be affected equally (Roger et al., 2011).

Pathogenesis: Errors in morphogenesis affecting the heart and much of the vascular system occur between weeks 2 and 6 in utero. The errors can range from faulty production of a crucial protein to skipping a step in the development process resulting in incomplete formation of structures or development of defective components of the structures, such as the excessive elasticity of blood vessels seen in Marfan syndrome. Regardless of the cause, these defects range in severity from innocuous anomalies that are only discovered by accident and have no effect on the individual to major defects that cause the death of a newborn child or the fetus in utero. Heart defects can initiate a series of events that change the ability of the heart to function over the life span of the individual, eventually causing premature death. Some of the most common defects allow a mixing of oxygenated blood coming from the lungs with deoxygenated blood coming from the systemic circulation. This abnormality is called a **shunt**. There are two types of shunts, each causing the heart to overwork. One type of shunt results in cyanosis due to a mixture of oxygenated and deoxygenated blood being pumped throughout the body; the other does not cause cyanosis but still increases the workload of the heart because oxygenated blood is pumped through the lungs repeatedly before going out to the body. The shunt that causes cyanosis is considered to be the more serious of the two. More information is presented with each specific defect.

Extraoral Characteristics: Each of the most common heart defects is described in this section along with information on pathogenesis important to understanding the impact of the defect on the function of the system or well-being of the individual.

- The ventricular septal defect (VSD) is a hole in the septal wall between the left and right ventricles. VSD is the most common congenital heart defect, occurring alone or in combination with other defects in about 25 to 40% of cases (Milliken & Galovich, 2011). Eighty percent of small VSDs close spontaneously during the first year of life (Milliken & Galovich, 2011). Initially, this defect may not cause symptoms of cyanosis. However, if the hole is large enough and is not corrected, cyanosis may occur. Cyanosis indicates that tissues are hypoxic, and symptoms of fatigue, shortness of breath, and tachycardia will be present to some degree. Individuals with chronic hypoxia for any reason tend to present with a characteristic clubbing of the fingertips (Fig. 8.11). Eventually, the right ventricle will hypertrophy to try and compensate for the increased workload, and when it can no longer adapt, right-sided CHF will occur. CHF is discussed later in this chapter. VSD leaves the affected individual at a higher risk for infective endocarditis, aortic valve prolapse, and blood clots in the circulation or emboli. An individual

BOX 8.5

Genetic Syndromes and Disorders Associated with Congenital Heart Defects

Trisomy 21
Trisomy 18
Trisomy 13
Cri du chat syndrome
Turner syndrome
Klinefelter syndrome
Marfan syndrome
22q11 Deletion syndromes
- DiGeorge syndrome
- Velocardiofacial syndrome (VCFS)

Noonan syndrome
Ehlers-Danlos syndrome
Rendu-Osler-Weber
Treacher Collins syndrome

FIGURE 8.11. Clubbing of the fingertips. Clubbing of the fingertips is associated with chronic tissue hypoxia. (From Bickley LS, Szilagyi PG. Bates' guide to Physical examination and history taking, 7th ed. Baltimore: Lippincott Williams & Wilkins, 1999.)

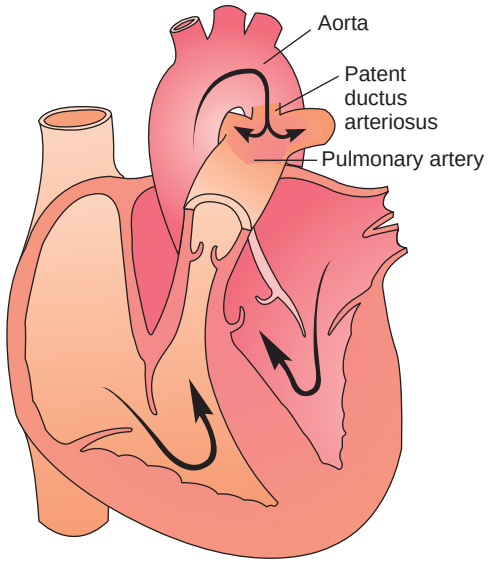

FIGURE 8.12. Patent ductus arteriosus. (From Pillitteri A. Maternal and child nursing. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

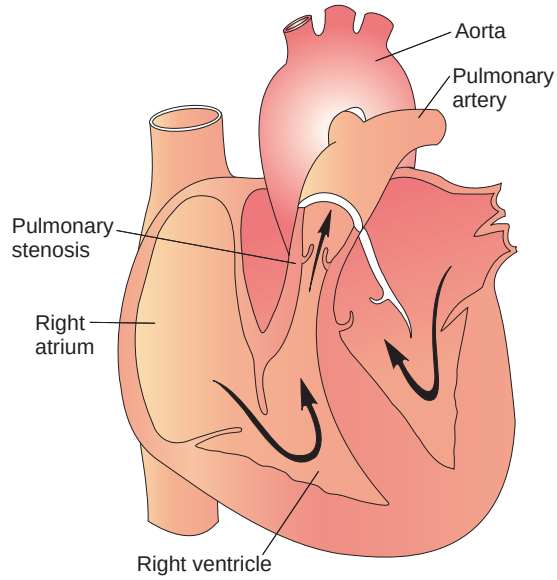

FIGURE 8.13. Pulmonary stenosis. (From Pillitteri A. Maternal and child nursing. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

with VSD will enjoy a normal life expectancy after correction of the defect (Milliken & Galovich, 2011).

- The atrial septal defect (ASD) is a hole in the wall between the right and left atria. ASDs account for about 10 to 15% of congenital heart defects (Markham & Cribbs, 2010). Most of these defects are asymptomatic unless they are large. If large, they may result in mixing unoxygenated blood with oxygenated blood as with the VSDs. Cyanosis and hypoxia along with right-sided CHF can result from a large untreated ASD. Symptoms include fatigue, shortness of breath, **dysrhythmias** (abnormal heartbeats), and clubbing of the fingers. These individuals are at a higher risk for infective endocarditis and emboli.
- Patent ductus arteriosus (PDA) occurs when the ductus arteriosus, which bypasses the lungs and allows blood from the right side of the heart to go directly into the circulation during fetal development, does not close within a few days after birth (Fig. 8.12). Delayed closure of the ductus arteriosus (sometimes taking several weeks or months) often occurs in premature infants, but full-term infants with PDA rarely have closure of the defect after the first several days. Symptoms include a **heart murmur** or abnormal heart sound and, later in life, the possibility of developing **pulmonary hypertension** (high blood pressure within the lungs) due to excessive blood flow to the lungs. Individuals with untreated PDA are at a higher risk for infective endocarditis and **arteritis** (infection of an artery).
- Pulmonary stenosis (PS) accounts for 8 to 12% of congenital heart defects (Syamasundar & Pflieger, 2010). PS is a narrowing of the pulmonary valve at the entrance of the pulmonary artery coming from the right ventricle (Fig. 8.13). PS is often caused by a fusion of the valve leaflets or cusps and symptoms depend on the extent of the defect. If the stenosis is severe, it will be difficult for the heart to pump blood into the lungs. The right ventricle will hypertrophy to compensate, and right-sided CHF may result. PS is the second most common congenital heart defect and often occurs in conjunction with other defects (Syamasundar & Pflieger, 2010).
- The tetralogy of Fallot (TOF) is seen in approximately 9 to 14% of cases and consists of four defects: (1) ventricular septal defect, (2) pulmonary stenosis, (3) overriding aorta, and (4) right ventricular hypertrophy (Roger et al., 2011) (Fig. 8.14). VSD and PS have been described above.

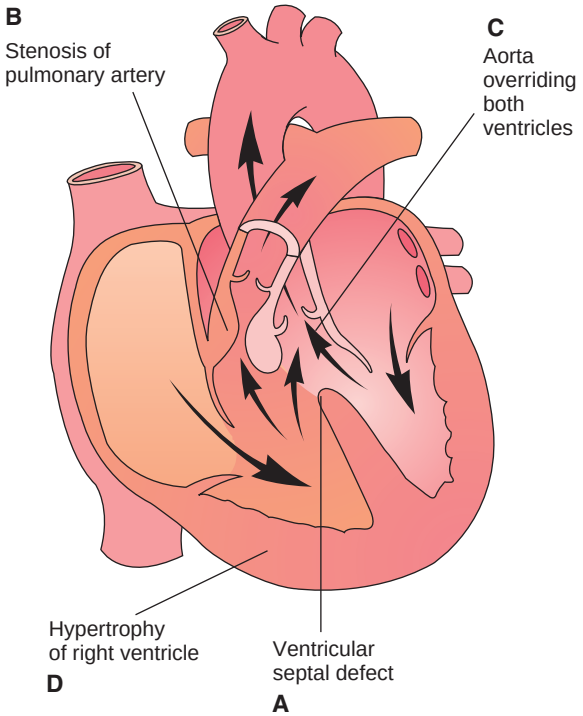

FIGURE 8.14. Tetralogy of Fallot. **A.** Ventricular septal defect (VSD). **B.** Pulmonary stenosis. **C.** Overriding aorta. **D.** Right ventricular hypertrophy. (From Pillitteri A. Maternal and child nursing. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

The overriding aorta is the hardest defect to visualize. Because of the hole in the septum, the aorta is displaced, and instead of opening in the left ventricle, it straddles the break in the septum and is partially in the right ventricle. The right ventricle hypertrophies because the heart has to work harder to get blood to the lungs through a stenotic pulmonary valve (PS). Often, children born with TOF have additional cardiac defects. The symptoms of this disorder depend on the severity of the stenosis and the size of the VSD. Larger VSDs are associated with cyanosis and hypoxia. Individuals with this disorder have shortness of breath, especially on exertion, poor growth, and clubbing of the fingers. Because they have chronic hypoxia, they also have a tendency to have **polycythemia** (an abnormal increase in the number of red blood cells). Polycythemia and its complications are discussed in Chapter 9. TOF increases the risk of infective endocarditis, emboli, brain abscesses due to embolization of bacterial vegetations formed in endocarditis, and acute episodes of cyanosis during which seizures, loss of consciousness, and sudden death are possible. Surgical correction will enable about 90% of individuals with TOF to survive into adulthood and maintain a satisfactory quality of life (Pettersen & Aparna, 2010).

- Coarctation of the aorta (COA) is a constriction of the aorta near the ductus arteriosus after the left subclavian artery branches off the aorta (Fig. 8.15). COA occurs in about 8 to 11% (Roger et al., 2011) of congenital heart defects; this defect is seen more frequently in males and often in conjunction with other defects (Rubin et al., 2008). COA presents with a difference in blood pressure and pulses in the upper body compared with those in the lower extremities. The heart must pump excessively hard to move blood through the constricted area. Pressure in the upper body is increased because the arteries supplying the upper body branch off the aorta before the area of constriction; the blood flow follows the path of least resistance and overflows into the upper body. The blood pressure in the lower extremities is diminished because a lower volume of blood is able to get past the constricted area. Pulses in the arms and neck appear to be bounding, compared with the weak pulses found in the lower extremities. Signs and symptoms in the upper body include left ventricular hypertrophy, dizziness, headache, and epistaxis. Weakness, pain, pallor, and coldness are found in the lower extremities. Untreated COA is associated with an increased risk of stroke, ruptured aortic and cerebral aneurysms, arteritis at the site of the constriction, or infective endocarditis at the aortic valve.

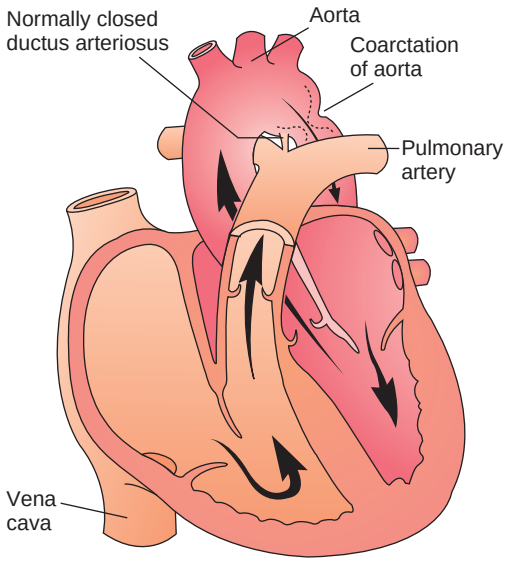

FIGURE 8.15. Coarctation of the aorta. (From Pillitteri A. Maternal and child nursing. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

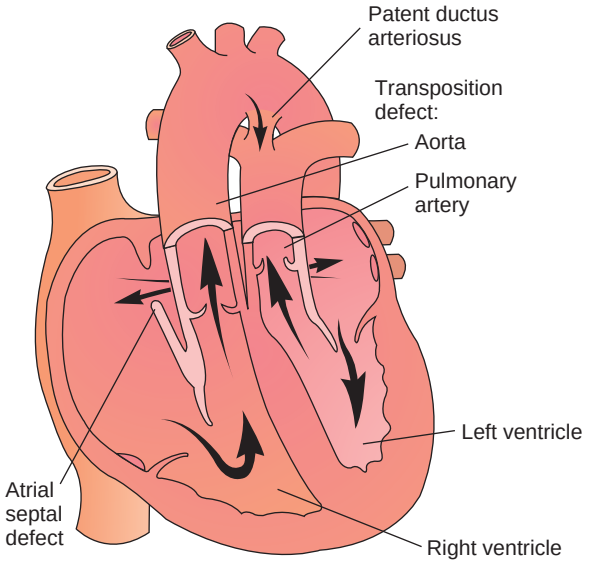

FIGURE 8.16. Transposition of the great arteries. (From Pillitteri A. Maternal and child nursing. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

- Transposition of the great arteries (TGA) occurs in 10 to 11% of heart defects. It is seen more often in males and in those born to mothers with diabetes (Roger et al., 2011). It is responsible for more than 50% of infant mortality due to heart defects that cause cyanosis (Rubin et al., 2008). TGA is exactly what its name implies, a complete reversal of normal anatomy. The aorta exits from the right ventricle, and the pulmonary artery exits from the left ventricle (Fig. 8.16). Most of the time, there is an associated septal defect that allows mixing of blood from the lungs and from the rest of the body; if not, this defect is lethal. The major presenting symptom in a newborn with this disorder is cyanosis and hypoxia.

Perioral and Intraoral Characteristics: Any of the congenital heart defects causing cyanosis will cause cyanosis in the soft tissues of the oral cavity, including the lips.

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

BOX 8.6

Indications for Prophylactic Antibiotic Premedication to Prevent Infective Endocarditis

Cardiac Conditions

- Prosthetic cardiac valve or prosthetic material used for cardiac valve repair
- Previous infective endocarditis
- Congenital heart disease (CHD)
  - Unrepaired cyanotic CHD, including palliative shunts and conduits
  - Completely repaired congenital heart defect repaired with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first 6 months after the procedure
  - Repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (both of which inhibit endothelialization)
- Cardiac transplantation recipients with valve regurgitation due to a structurally abnormal valve

Dental Procedures

Reasonable

Endocarditis prophylaxis is reasonable for patients with the highest risk of adverse outcomes who undergo dental procedures that involve manipulation of either gingival tissue or the periapical region of teeth or perforation of the oral mucosa.

Not Recommended

Endocarditis prophylaxis is not recommended for:

- Routine anesthetic injections through noninfected tissue
- Dental radiographs
- Placement or removal of prosthodontic or orthodontic appliances
- Adjustment of orthodontic appliances
- Placement of orthodontic brackets
- Shedding of deciduous teeth
- Bleeding from trauma to the lips or oral mucosa

From Nishimura RA, Carabello BA, Faxon DP, et al. ACC/AHA 2008 guideline update on valvular heart disease: focused update on infective endocarditis: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 2008;118:893, with permission.

Dental Implications: The presence of cyanosis in any individual should alert the dental professional to the possibility of a significant heart defect or disorder and should be investigated thoroughly prior to any treatment. Dental treatment modifications may include prophylactic antibiotic medication to prevent infective endocarditis (discussed later in this chapter), supplemental oxygen, stress reduction protocols, and caution in selecting local anesthetics. The American Heart Association's recommendations for prophylactic antibiotic regimens should be followed whenever indicated by the individual's medical history. Box 8.6 identifies cardiac conditions associated with an increased risk of endocarditis and lists dental procedures that do not require prophylactic antibiotics. Table 8.2 lists the medications recommended by the American Heart Association for prophylactic antibiotic regimens.

The patient should be educated about the relationship between oral bacteria/oral infections and infective

TABLE 8.2

Prophylactic Regimens for a Dental Procedure

Situation	Agent	Regimen: Single Dose 30–60 Minutes Before Procedure
Oral	Amoxicillin	Adults: 2.0 g Children: 50 mg/kg
Unable to take oral medications	Ampicillin or Cefazolin or ceftriaxone	Adults: 2.0 g IM or IV Children: 50 mg/kg IM or IV Adults: 1.0 g IM or IV Children: 50 mg/kg IM or IV
Allergic to penicillin or ampicillin—oral	Cephalexin[a] or Clindamycin or Azithromycin or clarithromycin	Adults: 2.0 g Children: 50 mg/kg Adults: 600 mg Children: 20 mg/kg Adults: 500 mg Children: 15 mg/kg
Allergic to penicillin or ampicillin and unable to take oral medications	Cefazolin or ceftriaxone[b] or Clindamycin	Adults: 1.0 g IM or IV Children: 50 mg/kg IM or IV Adults: 600 mg IM or IV Children: 20 mg/kg IM or IV

[a]Or use other first- or second-generation oral cephalosporin in equivalent adult or pediatric dosage.
[b]Cephalosporins should not be used in an individual with a history of anaphylaxis, angioedema, or urticaria with penicillins or ampicillin.
IM indicates intramuscular; and IV, intravenous.
From Nishimura RA, Carabello BA, Faxon DP, et al. ACC/AHA 2008 guideline update on valvular heart disease: focused update on infective endocarditis: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 2008;118:893, with permission.

endocarditis and how adequate home care regimens can decrease the risk of an autogenous (caused by the patient's own bacteria) infection.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Most congenital heart defects can be corrected with surgery, and most individuals have an excellent prognosis after successful correction of the defects. The prognosis for individuals with untreated or undiagnosed congenital heart defects depends on the type and severity of the defect. An unknown number of individuals may be living happily with slight congenital defects; on the other hand, it is not unusual for a premature death to be caused by an undiagnosed heart defect initially discovered at autopsy. The overall death rate from congenital cardiovascular defects was 1.2 per 1,000 babies in 2007. This is the leading cause of death in infants under the age of 1 year (Roger et al., 2011).

Heart Valve Defects

Disorders of the heart valves can be caused by a variety of factors; the most common causes are listed in Box 8.7. Defective heart valves are stenotic, insufficient, or both (Fig. 8.17). Stenotic heart valves do not open wide enough to let the normal amount of blood flow through them. The muscles of the chamber behind the valve hypertrophy to force blood through the narrow opening; when the muscles can get no larger, they relax, and the chamber becomes larger or dilates to hold the excess blood until the heart can pump it through the valve. Insufficient heart valves do not close completely and allow blood to **regurgitate** (flow back) into the chamber it just came from. The chamber behind the valve will hypertrophy to force more blood through the valve to make up for the backflow. When it cannot enlarge any more, the chamber will dilate so it can accommodate the increased amount of blood it is no longer efficiently moving through the valve. Blood flow through the defective valves is turbulent or rough and causes even more damage to the valves. As time passes, the heart weakens more, and CHF will result. Most valve defects present with an audible murmur. Murmurs caused by a valve defect are called **pathologic murmurs,** and each defect has a characteristic sound associated with it. The sounds are made by the noise the valve produces while it is working and by the turbulent blood flow through the valve. Benign or **physiologic murmurs** represent the normal functioning of the heart and

BOX **8.7** **Common Causes of Heart Valve Disorders**

- Rheumatic fever
- Congenital defects
- Infective endocarditis
- Syphilis
- Marfan syndrome
- Select pharmacologic weight loss aids (fenfluramine and dexfenfluramine)
- Degenerative changes that occur with age

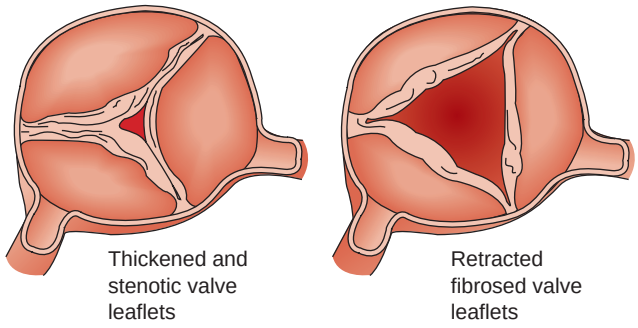

FIGURE 8.17. Valvular disease. Illustration showing a stenotic valve **(left)** that is thickened and narrowed and a valve that is insufficient **(right)** and unable to close completely.

are heard most often in young children because their chest walls are very thin. Individuals with physiologic murmurs often report "growing out of it" as they age. Physiologic murmurs do not need any type of treatment and are not associated with an increased risk for endocarditis.

Symptoms associated with valve defects are varied and depend on the type and severity of the defect. In general, stenotic valves result in less-oxygenated blood getting to the tissues. The person experiences shortness of breath, possibly chest pains, and cyanosis. Insufficient valves are usually better tolerated by the individual and may be asymptomatic for many years. Defective valves also have a tendency to put the heart at a high risk for dysrhythmia or abnormal heart rhythm, and many affected individuals present with an irregular heartbeat. In addition, the possibility of having areas within the heart where blood can pool for even short times increases the person's risk of developing a thrombus that can break free to travel to the lungs or other parts of the body. In 2007, about 23,313 people died from valve defects (Roger et al., 2011).

The presence of a heart valve defect increases the potential for developing infective endocarditis when a bacteremia is created while manipulating oral tissues. Research shows even daily home care will cause a bacteremia, especially in the presence of oral infections. Individuals with normal cardiac function may have no problem eliminating a transient bacteremia. However, individuals who have abnormal blood flow through their hearts may have an area where some blood can stay out of the main flow for a period of time, allowing any bacteria within that blood to attach to the endocardium. Or, the turbulent blood flow can damage the surface of the endocardium providing a rough spot that facilitates adherence of the bacteria, which then start reproducing. The American Heart Association no longer recommends prophylactic antibiotic medication prior to dental procedures for patients who have heart murmurs (Wilson et al., 2007; Nishimura et al., 2008). The dental hygienist has a professional responsibility to educate patients with valve disorders about the importance of maintaining a disease-free oral environment to decrease the risk of creating a bacteremia that can result in infective endocarditis.

The treatment for a valve defect depends on the type and severity of the defect. Minor defects may need no

treatment at all, while major defects might require surgical replacement of the valve. Medical treatment of valve disorders focuses on maintaining a normal heart rhythm, preventing the formation of blood clots and infection, and preventing CHF. In most cases of moderate-to-severe defects, an untreated individual will experience progression of the disorder into CHF and eventual death from heart failure or other complications. These individuals may be on daily prophylactic antibiotics and a consultation with their physician will be required prior to dental treatment to determine if an additional and different antibiotic will be necessary prior to dental procedures. In addition, they may be taking antithrombotics to decrease the chance of thrombus formation; if so, the coagulation status of the individual should be determined prior to dental procedures. Patients receiving medical therapy for heart valve defects should be evaluated for caries and periodontal disease because many medications used to control heart rate and rhythm cause xerostomia.

While heart valve defects can affect any of the heart valves, our discussion of valve disorders is limited to the more common disorders of the mitral and aortic valves.

NAME: Mitral valve prolapse (MVP)

Etiology: Although some cases of mitral valve prolapse (MVP) may be due to random errors in morphogenesis, inheritance appears to play a stronger role in the development of MVP.

Method of Transmission: MVP is thought to have an autosomal dominant pattern of inheritance. MVP can occur alone or in conjunction with other cardiac defects, and it is associated with many connective tissue disorders such as Marfan syndrome (Chapter 6), Ehlers-Danlos syndrome (Chapter 6), and osteogenesis imperfecta (Chapter 21).

Epidemiology: MVP is the most common valve defect encountered in a dental health care setting as about 5% of the population is affected (Rubin et al., 2008). Women are affected three times more often than men, but men have a higher risk for more severe complications. MVP is usually diagnosed after adolescence.

Pathogenesis: The abnormal connective tissue component of the valve leaflets results in stretching and ballooning of the valve back into the left atrium during ventricular contraction or systole (Fig. 8.18). In severe cases, the constant pressure may eventually result in further damage, requiring surgical replacement of the valve.

Extraoral Characteristics: MVP has been associated with a thin body type, thoracic deformities, and other connective tissue disorders. In most cases, this disorder is asymptomatic. However, a myriad of symptoms have been associated with MVP over the years, and there is much controversy about whether the symptoms are related to MVP or not and exactly what impact MVP has on the health of an individual. Some of the symptoms that have been associated with MVP are angina-like chest pain, palpitations, tachycardia, light-headedness, dyspnea (difficult breathing, shortness of breath), and fatigue.

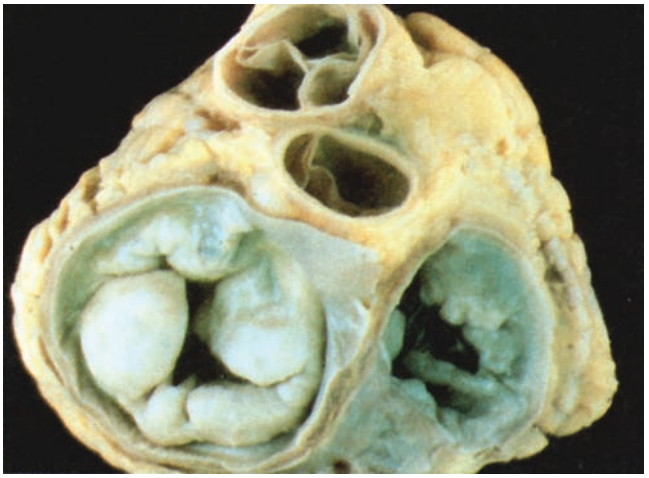

FIGURE 8.18. Mitral valve prolapse. A view of the mitral valve **(left)** from the left atrium shows stretched and deformed leaflets, which billow into the left atrial cavity. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

Perioral and Intraoral Characteristics: None

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: The American Heart Association no longer recommends prescribing prophylactic antibiotic medication for patients with MVP with or without regurgitation (Wilson et al., 2007; Nishimura et al., 2008).

Treatment and Prognosis: Medical treatment, if necessary, is directed toward relieving or eliminating the symptoms. Often, reducing or eliminating dietary stimulants such as caffeine and alcohol are all that is necessary to control the symptoms. In addition, beta-adrenergic blocking drugs that target palpitations, tachycardia, and chest pain may be prescribed if dietary restrictions alone do not suffice. Approximately 15% of those with MVP may develop damage severe enough to indicate replacing the mitral valve (Rubin et al., 2008).

NAME: Rheumatic heart disease

Etiology: Rheumatic heart disease is a sequela of rheumatic fever. Rheumatic fever is thought to be an autoimmune reaction that follows a throat infection caused by group A (beta-hemolytic) streptococcus.

Method of Transmission: Rheumatic heart disease is not transmitted from person to person; however, the triggering infection is caused by streptococci that is transmitted between persons.

Epidemiology: The incidence of rheumatic fever (and thus rheumatic heart disease) has declined in the United States. Death rates from rheumatic fever/heart disease are less than

1% in the United States (Chin et al., 2010). Rheumatic fever is a childhood disease usually occurring between the ages of 5 and 15. This disease is still a significant cause of death in less-developed countries. Rheumatic fever only follows 0.3 to 5% of untreated streptococcal throat infections, and rheumatic heart disease occurs in about 39% of those who have rheumatic fever (Chin et al., 2010). Rheumatic heart disease may not manifest for months or years after the initial rheumatic fever (Rubin et al., 2008).

Pathogenesis: Although there is an association between a particular streptococcal infection and rheumatic fever, it is not known exactly how the disease develops. The most widely accepted theory at this time is, after the original infection has resolved, antibodies that formed against the bacteria attack the cells of the host in a type II cytotoxic hypersensitivity reaction. The specific cells affected contain elements that are structurally similar to elements found in the bacteria, thus causing a cross-reaction between the antibodies and normal cells. The cells most likely to be affected are cardiac and smooth muscle cells. The end result is a systemic, immune-mediated inflammatory disease, or rheumatic fever. Rheumatic fever presents with a high fever; pain in the large joints; rash; subcutaneous nodules over the muscles of the wrist, elbow, ankle, and knee joints; and **carditis,** or inflammation of the heart about 1 to 4 weeks after a streptococcal throat infection. All of these manifestations, except the carditis, usually resolve within 3 months. Rheumatic heart disease is the chronic sequela of acute carditis and usually manifests as mitral or aortic valve damage observed clinically as a heart murmur.

Figure 8.19 illustrates the damage done to the mitral valve in rheumatic heart disease. As time passes, the damage becomes more extensive because of the continuing trauma from blood moving through the already damaged valve. Rheumatic heart disease remains the leading cause of mitral valve stenosis and valve replacement in adults in the United States today (Chin et al., 2010).

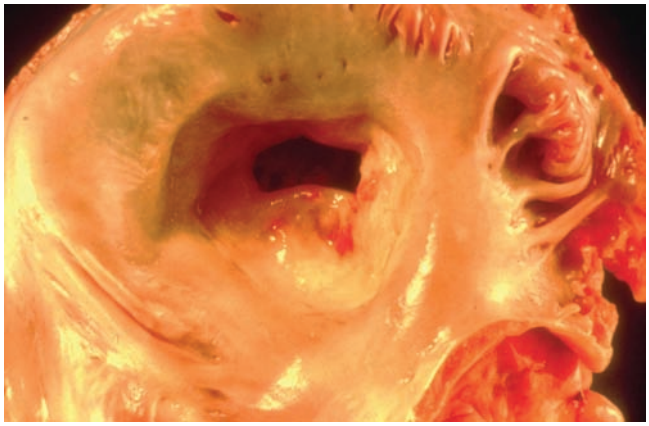

FIGURE 8.19. Rheumatic heart disease. A view of the mitral valve from the left atrium shows rigid, thickened, and fused leaflets with a narrow orifice, creating the characteristic "fish mouth" appearance of rheumatic mitral stenosis. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

Extraoral Characteristics: Red blood cells moving through damaged valves tend to be destroyed easily, therefore the patient may experience general symptoms associated with anemia such as fatigue, dyspnea, dizziness, pallor, and shortness of breath. They may also present with abnormal vital signs due to an irregular heart rhythm.

Perioral and Intraoral Characteristics: Not applicable

Distinguishing Characteristics: None

Significant Microscopic Features: The heart muscle develops a specific lesion in rheumatic fever, called an Aschoff body. The Aschoff body is a localized area of tissue necrosis surrounded by lymphocytes. This lesion is replaced with fibrous scar tissue as the disease resolves (Rubin et al., 2008).

Dental Implications: Rheumatic heart disease should be suspected whenever a patient reports a history of rheumatic fever. These individuals are sometimes given daily prophylactic antibiotics to prevent streptococcal infections that could lead to a recurrence of rheumatic fever. In addition, the patient may be receiving anticoagulation therapy, indicating the need to determine the coagulation status.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Preventing rheumatic fever is the best strategy for preventing rheumatic heart disease. Prompt diagnosis of any sore throat, especially those with accompanying fever, headache, and malaise, will optimize treatment of streptococcal infections and help prevent most cases of rheumatic fever. Prompt diagnosis and treatment of rheumatic fever can limit the severity of symptoms and decrease the potential for severe permanent heart damage. An individual who has once had rheumatic fever is at a considerably higher risk of a recurrence, which would lead to even more heart damage. In 2007, 3,201 individuals died from rheumatic fever or rheumatic heart disease (Roger et al., 2011).

NAME: Infective endocarditis

Etiology: Bacteria, especially *Staphylococcus* and *Streptococcus*, are the most common causative agents associated with infective endocarditis. Gram-negative bacilli, yeasts, and fungi have also been found (Rubin et al., 2008; Porth, 2011).

Method of Transmission: Infective endocarditis is considered an autogenous infection; therefore, it is not transmissible from person to person. Individuals must have bacteria in their bloodstream (bacteremia) before they can develop infective endocarditis. In most cases, these are transient or short-lived bacteremias, which are eliminated by the body in the natural course of immune system and bodily functions. The infective agents are introduced into the bloodstream of the patient in a variety of ways ranging from illegal intravenous drug use with dirty needles to legitimate medical care involving the use of intravascular catheters to brushing and flossing at home to remove dental biofilm.

Epidemiology: The incidence of infective endocarditis in the United States is about 2 to 4 cases per 100,000 people. The disease occurs two to three times more frequently in males than in females. The frequency of infections occurring in those over 60 years of age is increasing, accounting for 25 to 50% of all cases (Brusch, 2009). Of those cases occurring in adults, more than half occur in adults with no underlying cardiac condition, while in children, most cases occur in the presence of a congenital heart defect (Rubin et al., 2008).

Pathogenesis: The development of infective endocarditis depends on the following factors (Brusch, 2009):

- Presence of a bacteremia
- Adherence of the bacteria or other causative agent to the valve
- Invasion of the valve leaflets by the organism

Vegetative growths or clumps of organisms, cellular debris, and clotted blood appear on the valve leaflets after the organism establishes itself (Fig. 8.20). These vegetations destroy the connective tissues of the valve leaflets. The vegetations adhere loosely to the endocardial surfaces and frequently break free, becoming emboli. The emboli travel to distant parts of the body and may cause infarcts (areas that become necrotic because the blood supply is obstructed by a clot or in this case a mass of bacteria) and abscesses in many organs including the brain, lungs, and kidneys.

Extraoral Characteristics: The disease can manifest as an acute or subacute infection. The acute manifestation presents with high fever, chills, severe shortness of breath, and fatigue associated with CHF (discussed later in this chapter). Asymmetrical joint pain, a red macular rash, and petechiae on the hands, feet, chest, and abdomen may also be observed.

The subacute infection has a less dramatic course characterized by low-grade fever, flu-like symptoms, anorexia, and weight loss. A detectable heart murmur is present in about 99% of cases (Brusch, 2009). Chest pain, joint pain, and back pain are frequently reported. Neurologic symptoms similar to those associated with a stroke are often present. CHF occurs more gradually with the subacute form of the infection.

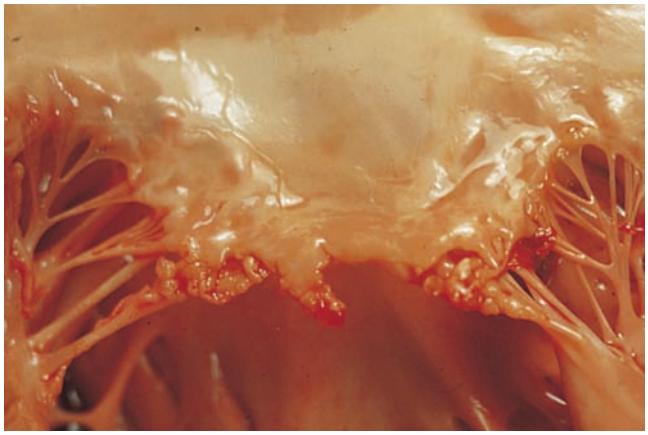

FIGURE 8.20. Infective endocarditis. The mitral valve shows destructive bacterial vegetations that have eroded through the free margins of the valve leaflets. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

Perioral and Intraoral Characteristics: **Petechiae** (minute hemorrhagic spots) may be found on any of the oral mucosal surfaces, especially the soft palate and buccal mucosa (Brusch, 2009).

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: The causative organism can be cultured from the blood of the individual. Treatment is not successful until all signs of the organism are eliminated from the blood and from any thrombi or emboli in the body.

Dental Implications: The American Heart Association recommends that individuals with a prior history of infective endocarditis receive prophylactic antibiotic coverage before many dental procedures (Table 8.2 and Box 8.6). Gingival and periodontal infections are the most common source of transient bacteremias. Even more interesting is the fact that surveys have shown few individuals who are at risk for infective endocarditis are aware of the importance of maintaining good oral health as a method of preventing this disease (Brusch, 2009). Dental professionals can make a significant impact in this area by identifying those individuals at risk for infective endocarditis and stressing the importance of maintaining oral health to prevent the likelihood of a significant bacteremia being produced.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment focuses on two areas: (1) identifying and eliminating the causative organism and (2) managing complications due to valve damage. Antibiotic therapy is the treatment of choice to destroy bacterial organisms. Other causative organisms are treated with drugs that target those specific organisms. Surgery may be necessary to eliminate abscesses that develop in other areas of the body. Heart valve damage may be so severe that one or more valves must be replaced to manage the CHF that occurs.

The prognosis for infective endocarditis varies; untreated disease is invariably fatal. The American Heart Association estimated that 2,420 individuals died from infective endocarditis in the United States in 2007. In addition, there were 27,000 hospital discharges that listed infective endocarditis as a primary or secondary diagnosis (Roger et al., 2011). Relapses are common and are more frequent among those who abuse intravenous drugs, have congenital heart defects or prosthetic heart valves, or have had a previous episode of infective endocarditis (Brusch, 2009).

NAME: Congestive heart failure (CHF)

Etiology: CHF occurs when the heart is no longer able to move an adequate amount of blood throughout the body, allowing body tissues to become congested with retained fluids. This is most commonly caused by coronary artery

disease, hypertension, congenital heart defects, defective heart valves, chronic obstructive pulmonary disorders, and anything else that causes the heart to overwork or impairs its function (Grossman & Brown, 2011). In women with coronary artery disease, diabetes appears to be a major risk factor for CHF (Roger et al., 2011).

Method of Transmission: Not applicable

Epidemiology: In 2008, approximately 5,700,000 individuals in the United States were living with CHF (Roger et al., 2011). The disorder affects men more than women, until the age of 75 when it equals out. (Grossman & Brown, 2011). The risk of developing CHF increases with age; 10 of every 1,000 individuals over the age of 65 are affected (Roger et al., 2011). Approximately 75% of all cases of CHF occur in conjunction with chronic hypertension (Roger et al., 2011).

Pathogenesis: CHF is the end result of many chronic and some acute conditions that cause progressive weakening of the heart muscle. CHF manifests as an inability of the heart to pump enough blood to all of the tissues of the body. The edema that results is caused by the decreased cardiac output, which, in turn, causes a decrease in the volume of blood the kidneys can filter. Any decrease in the rate of filtration by the kidney eventually triggers the release of higher-than-normal levels of aldosterone from the adrenal glands. High levels of aldosterone cause sodium reabsorption by the kidneys and fluid retention. As this disease progresses, individuals become more and more incapacitated as less and less blood reaches their tissues. There are several ways to classify heart failure; however, left- and right-sided heart failure will suffice for the purposes of this text.

Left-sided heart failure reflects the inability of the heart to move adequate blood from the pulmonary circulatory system into the systemic circulatory system. Symptoms associated with pulmonary edema (listed below) result from left-sided heart failure. Right-sided heart failure reflects the inability of the heart to move the blood returning from the venous circulation into the pulmonary circulation for oxygenation. Symptoms associated with peripheral edema and edema of central organs (listed below) result from right-sided heart failure. One way to remember which side is associated with which symptoms is to associate "left" with "lungs" and then right must be associated with return of the venous circulation.

Extraoral Characteristics: Symptoms associated with heart failure are initially confined to one or the other side of the heart. However, as the disease progresses, both sides of the heart are eventually involved.

Left-sided heart failure results in pulmonary edema. Symptoms of this include impaired gas exchange that causes an inability to perform normal activities, cyanosis, **paroxysmal nocturnal dyspnea** (acute episodes of shortness of breath and coughing that occur during the night), and **orthopnea** (an inability to breathe comfortably in a supine position).

Right-sided heart failure results in peripheral edema, which most notably occurs in the lower extremities during the initial stages of the disease (Fig. 8.21). Slowing of

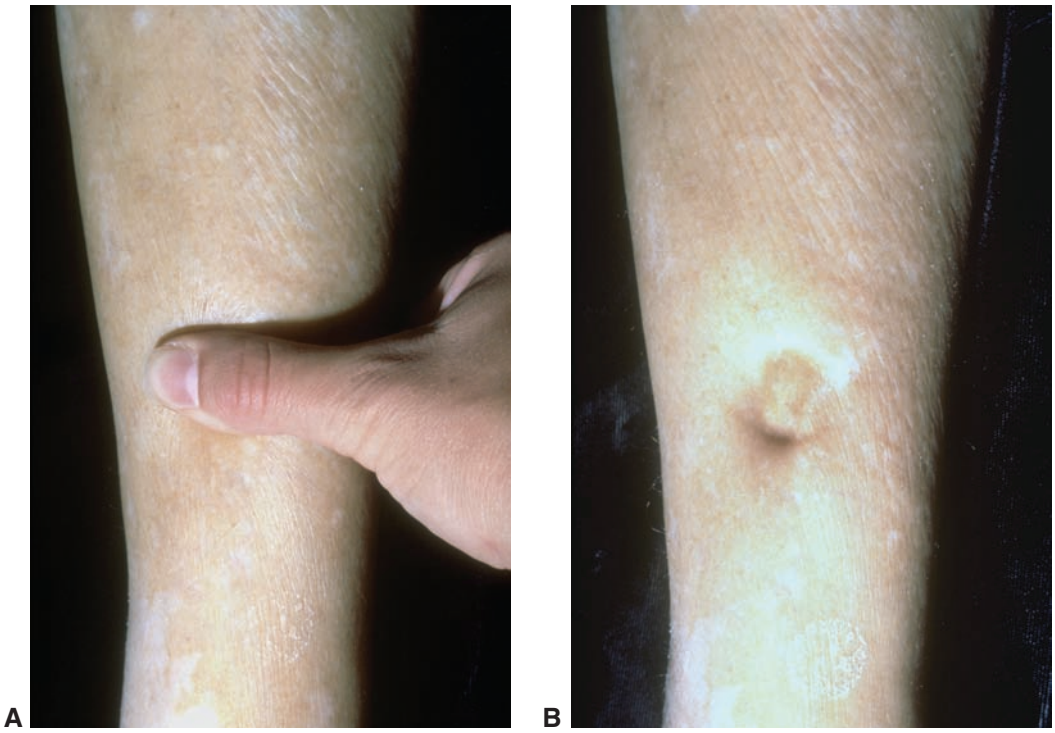

FIGURE 8.21. Pitting edema of the leg. **A.** In a patient with congestive heart failure, severe edema of the leg is demonstrated by applying pressure with a finger. **B.** The resulting "pitting" reflects the inelasticity of the fluid-filled tissue. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

the venous blood flow back to the heart causes blood and fluid buildup in the abdominal organs as well. Liver failure, enlargement of the spleen, and gastrointestinal symptoms of anorexia, weight loss, and severe anemia will manifest later in the disease progression. Increased urine output at night **(nocturia)** occurs because the effects of gravity are removed when in the supine position and the fluid can flow more easily back to the heart and through the kidney.

Perioral and Intraoral Characteristics: Cyanosis of the lips and oral mucosal surfaces is possible in both right or left heart failure and are associated with any severe or end-stage disease. In severe right-sided heart failure, the jugular veins become distended and can be observed when the individual is in an upright position, as when an extraoral examination is done. Although not associated with CHF, xerostomia caused by medication taken to manage the disease is a consistent finding.

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: Modifications in dental care depend on the stage of the disease and the symptoms present in the individual. Modifying the patient's chair position to semi-upright or upright might be indicated, as well as providing supplemental oxygen to aid in breathing. The patient should be evaluated for xerostomia and caries prevention therapies.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment focuses on removing the cause of the heart failure if possible; for example, repairing a defective heart valve or replacing it, repairing a septal defect, managing hypertension, or treating a pulmonary disorder. Medical management focuses on relieving the symptoms and maintaining quality of life for the individual. Drugs can help to decrease the levels of aldosterone, remove excess fluid from the body, and increase the force of the heart's contractions.

Approximately 56,565 individuals died from CHF in 2007. CHF was listed as the cause of death or contributing to the cause of death on approximately 277,193 death certificates across the United States in 2007 (Roger et al., 2011).

Dysrhythmias

Dysrhythmias are abnormal heart rhythms or beats. Cardiac dysrhythmias occur in a high percentage of the population. These abnormalities are associated with the conduction of abnormal or inappropriate electrical impulses through the heart muscle and can be caused by scar tissue from myocardial infarctions, valve dysfunction, or other cardiac disorders. Examples of irregular heartbeats include tachycardia (fast heartbeat), bradycardia (slow heartbeat), and ventricular and atrial fibrillation.

Tachycardia and bradycardia can occur occasionally or frequently, and the symptoms can range from insignificant to life threatening. If symptoms such as shortness of breath or chest pain occur, the individual should receive treatment.

Ventricular fibrillation occurs when there is an irregular spread of impulses through the bundle of His up to the Purkinje fibers. This leads to twitching of the heart muscle and little or no blood being pumped through the circulatory system. Cardiac arrest will occur if ventricular fibrillation is not stopped.

Atrial fibrillation is caused by erratic conduction of impulses from the SA node, which results in uncoordinated atrial contractions. Atrial fibrillation is associated with an increased risk of stroke.

Medications such as digoxin or beta-blockers may be used to manage abnormal heart rhythms. Serious disorders are treated with cardiac pacemakers and implanted defibrillators that normalize the beat and, if necessary, shock the heart to stop fibrillation.

The dental professional has the opportunity to identify abnormal heart rhythms while obtaining vital signs and through discussion of the patient's medical history. Often, patients who have abnormal heart rhythms will complain of heart palpitations where the heart appears to stop and then start abruptly. Because many dysrhythmias are caused by an underlying cardiac condition, it is important to refer these patients to their physician for evaluation. The presence of an implanted pacemaker or defibrillator does not indicate the need for prophylactic antibiotic coverage unless warranted by the underlying cardiac condition.

SUMMARY

- Cardiovascular abnormalities can be genetic or they may be acquired during morphogenesis or at some other time during life.
- Turbulent, as opposed to laminar, blood flow contributes to cardiovascular injury, infection, or disease.
- Atherosclerosis is a major risk factor for most acquired chronic cardiovascular disorders and is associated with both modifiable and unmodifiable risk factors.
- Oral infections increase the amount of circulating inflammatory products, which may contribute to endothelial injury and encourage the development of atherosclerosis.
- Hypertension affects one of every three American adults. Both the etiology and pathogenesis are complex, but there are known risk factors that can be altered to prevent or limit the extent of the disease and its complications or sequela.
- Coronary heart disease (CHD) occurs when the heart muscle is not supplied with enough oxygen to meet its needs. The two basic types of CHD are chronic ischemic heart disease and acute coronary syndromes.
- Abdominal aortic aneurysm (AAA) is a sequela of atherosclerosis that involves the weakening and bulging of the arterial wall. The most significant complications of AAA are rupture and thrombus formation.

- Raynaud disease/phenomenon is caused by vasospasms in the small vessels of the skin of the fingers and toes and, less often, the nose and ears.
- Deep venous thrombus is characterized by the formation of thrombi in the deep veins of the legs. Aside from pain, inflammation, and swelling of the lower extremities, DVT can result in the creation of emboli that can travel to the lungs as pulmonary emboli.
- Stroke is a sequela of hypertension and atherosclerosis. Strokes occur when there is ischemia to an area of the brain either because of a thrombus, embolus, or intracranial hemorrhage. Blood flow to the area must be restored quickly to reduce the amount of permanent damage.
- Transient ischemic attacks (TIA) are temporary episodes of ischemia that often warn of, or precede, a stroke.
- Congenital heart defects can be very slight or they can be so severe that they cause death in utero or during the neonatal period. The most common congenital heart defect is the ventricular septal defect (VSD).
- Cyanosis is associated with some congenital heart defects and is a sign that there is mixing of blood returning from general circulation with blood from the pulmonary circulation. The heart must work harder to get oxygen to all of the body's tissues. CHF is a possible result of these conditions.
- Heart valve disorders can cause valvular stenosis, insufficiency, or both. The most common disorder is mitral valve prolapse, which can occur with or without regurgitation. Heart valve defects may result in CHF.
- Infective endocarditis is the result of a bacteremia. Often, bacteria enter the blood by way of the oral cavity through trauma or everyday oral hygiene care. Oral infections, particularly periodontal infections, increase the risk of creating bacteremia during everyday oral care and eating.
- Rheumatic heart disease is the result of an error in the immune system response that causes antibodies that have formed against streptococcal bacteria from a throat infection to attack and damage the tissues of the heart, causing carditis. While the carditis usually resolves, there may be permanent damage to the heart valves.
- CHF is the end result of many cardiovascular disorders that cause the heart to overwork to move blood throughout the body. Eventually, the heart cannot compensate for the added work by hypertrophy or other means; the contractions begin to weaken; fluids build up in the lungs, extremities, or both; and the heart fails.
- Dysrhythmias or abnormal heartbeats result from the abnormal conduction of electrical impulses through the heart muscle. A history of dysrhythmia can be associated with many types of heart defects or damage and should be thoroughly investigated prior to performing dental treatment.
- Dental professionals must prepare accurate health information regarding cardiovascular disorders because some of the disorders increase an individual's risk for infective endocarditis.

CHAPTER REVIEW

Case Study 8.1

Your first appointment for the day is with a 7-year-old boy named Ben. You have not met Ben before, but you know his father and mother. Ben presents as a healthy-looking young boy who appears rather tall for his age. You are aware his father has Marfan syndrome, but neither his father nor his mother has said Ben has Marfan syndrome. As you are going over the medical and dental history with Ben's mother, you are trying to think of how to ask the questions you think are necessary.

1. What questions do you think you need to ask Ben's mother?
2. What specific heart or circulatory disorders are associated with Marfan syndrome?
3. What are possible adverse health effects Ben might suffer if his oral health is poor?
4. Are there any contraindications for providing dental hygiene therapy for Ben if he has Marfan syndrome?
5. What patient education topics would be appropriate for Ben and his family if he has a heart disorder associated with this syndrome?

Case Study 8.2

Your last patient of the day is Ms. Wentworth, 70 years of age. You have reviewed her medical/dental history and noted the following: height—5′5″, weight—150 lb, former smoker—quit 5 years ago, reports health as "fair," no prescription medications, over-the-counter (OTC) calcium and multivitamin supplements, last physical—10 years ago. Her vital signs were within normal limits except for her blood pressure, which was 144/92. As you are discussing your findings with her, you observe the condition seen in Figure 8.22.

FIGURE 8.22.

1. What information can you gather from her health history and what does the information mean?
2. What follow-up questions would be appropriate for this patient?
3. During your follow-up questioning, you discover she feels her health is only fair because she is no longer able to take her dog for their usually long walks along the river because her legs hurt. What does this information add or how does it help you?
4. Does the condition pictured in Figure 8.22 help you in any way? How? What follow-up questions would you want to ask?
5. Assuming you have shared your observations with the dentist and discussed them together, how will you inform your patient of your findings? What will you tell her?
6. Will you provide dental hygiene care for this individual today? What recommendations or referrals will you provide her with?

For answers and additional review activities, log in to **thePoint.lww.com**

Critical Thinking Activities

1. What do you think the role of a dental hygienist should be in regard to educating patients about cardiovascular diseases? Do you feel the hygienist should only relate information that is germane to the link between oral and cardiovascular health, or do you think the hygienist should be able to discuss other aspects of cardiovascular health such as diet and exercise?
2. Your office receives a call from Mrs. Wiggins, a 65-year-old patient of record. She is complaining of severe pain in her jaw on the left side. She reports the pain started rather suddenly and has not diminished over the last hour. She would like an appointment as soon as possible because she does not feel she can tolerate it much longer. Describe how you think this call should be handled.

Portfolio Possibilities

- Develop a patient-centered fact sheet dealing with why it is important for an individual who is at risk for infective endocarditis to have excellent oral health. This can be made available to the dental hygiene clinic patients and can be used as a handout at health fairs and other community events.
- Gather information on prehypertension and hypertension. Put together a fact sheet for your patients discussing what these are and how they can impact the individual's health. Discuss the implications of prehypertension and suggest some lifestyle changes that might help to control or eliminate it. State why your practice is committed to screening for hypertension and emphasize the need for a medical evaluation to make a definitive diagnosis. This will make an excellent handout for your clinic or dental office and will help the patients remember what they have been told.

Media Menu

Web Sites

American Heart Association
http://www.heart.org

Congenital Heart Defects Tools and Resources
http://www.heart.org/HEARTORG/Conditions/CongenitalHeartDefects/CongenitalHeartDefectsToolsResources/Congenital-Heart-Defects-Tools-and-Resources_UCM_002031_Article.jsp

Colgate Professional Education: Periodontal Disease and Overall Health: A Clinician's Guide
http://www.colgateprofessional.com/professionaleducation

Multimedia Resources

Congenital Heart Defects Media Library
http://medmovie.com/mmdatabase/mediaplayer.aspx?Message=VG9waWNpZD0wO0NsaWVudElEPTEwMztWZXJuYWN1bGFySUQ9MQ%3D%3D-p1aJeSO1y4M%3D

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Take advantage of additional online resources to help you study and ace your exams!

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- Additional case studies and answers
- Interactive quiz bank with answer feedback
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- Expanded Media Menu with direct links to related Web sites and multimedia resources
- Supplemental references

thePoint Online resources and links are available at *http://thepoint.lww.com/DeLong2e*

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Chapter 8 **LESION/CONDITION SUMMARY TABLE**

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Atherosclerosis	Multifactorial: genetic, environmental	Formation of plaques in the tunica interna causes increased risk of clot formation, leads to hypertension.	Presents as coronary artery disease, peripheral artery disease (PAD), aneurysm, hypertension, and more; may observe xanthelasma	N/A	Eliminate/manage risk factors: medications to lower lipids, cholesterol, and hypertension; life style modifications; control diabetes. Manage complications such as coronary heart disease, aneurysm, PAD, etc.	Evaluate for xerostomia and other medication side effects or interactions, identify at-risk individuals, refer for evaluation if xanthoma is present, and educate on oral–systemic link.
Hypertension	Primary Multifactorial: genetic, environmental Secondary Sequela of other disease	Primary: Atherosclerosis narrows arteries and decreases the ability to dilate to lower pressure. May result in hypertensive heart disease	Prehypertension, hypertension, risk factor for stroke, CHD, kidney disease, thromboembolic disorders, and more	N/A	Treatment: modify lifestyle, lose weight, control diabetes, tobacco cessation, medications to lower pressure, lipids, and cholesterol, and reduce vasoconstriction and lower heart rate.	Establish guidelines for when to treat or postpone treatment for patients with hypertension, evaluate for xerostomia, prevent orthostatic hypotension, and use caution with local anesthetics containing vasoconstrictors.
Coronary Heart Disease (CHD)	Atherosclerosis	Chronic ischemic heart disease (stable angina, silent ischemia): one or more of coronary arteries 75% or more occluded Acute coronary syndromes: necrosis of myocardial cells or sudden death	Angina: substernal chest pain may radiate to the left arm or jaw. Silent: mild symptoms can be confused with indigestion or dismissed altogether. Myocardial infarction: symptoms range from severe crushing pain to no pain; may have vomiting/ nausea/copious sweating and dyspnea. Sudden death: usually associated with ventricular fibrillation	N/A	Chronic ischemic: relieve symptoms, prevent myocardial infarction; eliminate risk factors such as smoking, manage conditions such as diabetes, high cholesterol, and hypertension. Medications can reduce cardiac workload; reduce chance of thrombus formation, lower blood pressure and cholesterol levels. Acute syndromes: damage from lack of oxygen can be reversed if blood flow is restored quickly and heart muscle begins to function correctly. Otherwise, cells undergo necrosis with eventual scar formation and reduced functional capacity.	Consult with patient's cardiovascular physician to determine the appropriate time to initiate dental treatment after an MI, no treatment for unstable angina, stress reduction, supplemental O_2 during appointment, manage side effects of medications, determine coagulation status, use local hemostatic measures, patient education on oral–systemic link, and prepare for medical emergency.
Peripheral Artery Disease (PAD)	Atherosclerosis	Narrowed arteries in lower extremities decrease blood flow and increase the risk of thrombus formation	Calf pain on walking, aching pain or slight numbness, loss of hair on the leg, atrophy of muscle, weak pulses	N/A	Address risk factors: eliminate smoking, control diabetes, increase physical activity; medications can control hypertension, lower cholesterol, reduce risk of clot formation. Bypass surgery or stent placement may be necessary in severe cases.	Determine coagulation status, use local hemostatic measures, evaluate for side effects of medications (xerostomia, gingival hyperplasia), tobacco cessation counseling/support. Identify at-risk individuals and refer for evaluation.
Abdominal Aortic Aneurysm (AAA)	Atherosclerosis and hypertension	The artery wall becomes weak, thins, and expands, ending in rupture and death.	Most have no symptoms but may present with pain in the back or groin, dysphagia, and pulsating mass near umbilicus.	N/A	Small aneurysms may be monitored; large must be repaired or replaced surgically. Medications to lower blood pressure may slow enlargement; antithrombotics may be given to reduce risk of clot formation.	Evaluate the patient for side effects of medications, determine coagulation status, use local hemostatic measures, educate on oral–systemic link, and identify at-risk individuals from medical/ dental history and refer for evaluation.
Raynaud Disease (primary)/ Phenomenon (secondary)	Idiopathic/ associated with other diseases or traumatic injuries	Ischemia of cells in fingers, toes, ears, nose caused by capillary vasospasms	Color changes pale then cyanotic, numbness, tingling then turns red with pain, throbbing and altered sensation	N/A	Avoid precipitating factors such as cold and stress, vasodilators like calcium channel blockers may help, and severe cases may need surgery to cut the sympathic nerve supply to the area.	Refer to a physician for evaluation if the patient reports symptoms associated with Raynaud; for side effects of any prescribed medications.

continues

Chapter 8 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Thromboembolic Venous Disorders Deep Venous Thrombosis (DVT) Pulmonary Embolism (PE)	Endothelial injury, blood stasis, slow blood flow, hypercoagulability	Clot forms and either occludes the vessel or becomes embolism and travels to other areas such as the lung.	DVT: deep muscle pain and swelling in the legs, fever, and other signs of systemic inflammation possible PE: pain, dyspnea	N/A	Antithrombotic therapy to reduce clot formation, fibrinolytic agents to break up existing clots, Physical exercise, support stockings, and air compression devices help to prevent clot formation.	Determine coagulation status, use local hemostatic measures, and prepare for managing emergencies.
Stroke	Ischemia/ hemorrhage	Ischemia results from obstruction of the vessel due to atherosclerosis thrombus or embolus; hemorrhage is due to trauma, hypertension, or aneurysm rupture.	Full or partial paralysis of one side of the body, blurred vision, slurred speech, loss of balance Hemorrhage may cause nausea, vomiting, headache, coma, and death.	N/A	Ischemic strokes need to be treated quickly, within 3–4.5 hours. Thrombolytic drugs may be used to reestablish blood flow. Hemorrhagic stroke patients are monitored for intracranial pressure and may require surgery to remove hematomas pressing on the brain.	Manage side effects of medications, determine coagulation status, and use local hemostatic measures; evaluate the patient for poststroke physical abilities to determine necessary home care modifications.
Congenital Heart Defects	Genetic, developmental and environmental factors	Defects develop during weeks 2–6 in utero.	Defects manifest with or without cyanosis, and differing levels of other symptoms such as shortness of breath, stunted growth, clubbing of fingers, anemia, etc.	N/A	Surgical repair of defect, medical management of symptoms with medications	Identify patients with unrepaired cyanotic defects who should be covered with prophylactic antibiotics, educate about oral–systemic link, determine coagulation status, use local hemostatic measures, and use caution selecting local anesthetics.
Mitral Valve Prolapse (MVP)	Genetic, developmental and environmental factors	Weakening of the valve leaflets with stretching and ballooning into the left atrium Some have regurgitation.	Detectable murmur, chest pain, palpitations, tachycardia, dyspnea, fatigue	N/A	Manage symptoms with medications to lower heart rate and blood pressure, reduce or eliminate caffeine and alcohol; severe disease may require replacement of the valve.	Increased potential for infective endocarditis, educate about oral–systemic link, antibiotic coverage no longer recommended. If the valve has been replaced: determine coagulation status, use local hemostatic measures, and prophylactic antibiotic coverage is necessary.
Rheumatic Heart Disease	Autoimmune reaction following streptococcal throat infection	Valve leaflets are damaged and fuse together, causing a stenotic, insufficient valve.	General symptoms of anemia, abnormal vital signs	Aschoff body: localized area of tissue necrosis surrounded by lymphocytes	Treat throat infections so they do not lead to rheumatic fever. Prompt treatment of rheumatic fever can limit damage to the heart.	Increased potential for infective endocarditis, educate about oral–systemic link, antibiotic coverage no longer recommended. If the valve has been replaced: determine coagulation status, use local hemostatic measures, and prophylactic antibiotic coverage is necessary.
Infective Endocarditis	Bacteria, gram-negative bacilli, fungi, yeasts	Bacteria (microbes) enter blood causing bacteremia, bacteria adhere to the valve, and organisms invade the valve leaflet.	Acute: high fever, severe dyspnea, congestive heart failure, joint pain, rash, and petechiae (hands, feet, chest, abdomen, oral mucous membranes) Subacute: less dramatic, low-grade fever, flu-like symptoms, weight loss, heart murmur	Causative organism can be cultured from the blood.	Identify and eliminate the organism. Manage the complications due to valve damage. Individuals who have had infective endocarditis are at a very high risk of developing it again.	Educate about oral–systemic link, antibiotic coverage no longer recommended. If the valve has been replaced: determine coagulation status, use local hemostatic measures, and prophylactic antibiotic coverage is necessary.

Chapter 8 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Congestive Heart Failure (CHF)	Sequela of other cardiovascular disorders such as defective valves, hypertension, and congenital heart defects	The heart can no longer compensate for increased workload and cannot move sufficient blood allowing the buildup of fluid in body tissues.	Left-sided failure: pulmonary edema, orthopnea, cyanosis, nighttime coughing spasms Right-sided failure: peripheral edema, fluid retention in the abdomen and organs, anemia, nocturia	N/A	Eliminate the cause of heart failure, medically manage the symptoms with medications that decrease aldosterone, increase force of contractions, and remove the excess fluid (diuretics).	Evaluate the patient for side effects of drugs, provide supplemental O_2, and adjust patient chair position to facilitate easy breathing. May require assistance from a caregiver to accomplish daily home care
Dysrhythmia	Abnormal or inappropriate conduction of electrical impulses through the heart muscle	Associated with scar tissue in the heart, damaged valves, and other heart conditions and defects	Presents as irregular heartbeat, palpitations, tachycardia, bradycardia, and atrial and ventricular fibrillation	N/A	Medical management with beta-blockers and digoxin can help to regulate rhythm. Pacemakers and implanted defibrillators may be used also.	Identify patients with abnormal heart rhythm while obtaining vital signs and refer for evaluation; no prophylactic coverage is necessary unless needed for an underlying cardiac condition.

CHAPTER 9

Blood Diseases

KEY TERMS

Anemia
Ataxia
Blastic cells
Erythrocytes
Erythropoiesis
Glossitis
Hemarthrosis
Hematocrit
Hematopoiesis
Hematopoietic system
Hematuria
Hemolytic
Hemostasis
Hypercoagulation
Jaundice
Pernicious anemia
Phlebotomy
Plummer-Vinson syndrome
Pluripotential stem cells
Proprioceptive

LEARNING OUTCOMES

1. Define and use the key terms listed in this chapter.
2. Briefly describe how blood cells are produced and what regulates their production.
3. Discuss how the body achieves hemostasis.
4. Describe general oral signs and symptoms that might indicate a systemic condition such as a blood disorder.
5. State the etiology, method of transmission, and pathogenesis of the blood disorders discussed in this chapter.
6. Describe the extraoral, perioral, and intraoral characteristics of disorders involving erythrocytes, leukocytes, and the hemostatic (coagulation) process.
7. Describe the dental implications of disorders involving erythrocytes, leukocytes, and the hemostatic (coagulation) process and discuss possible dental/dental hygiene treatment modifications.
8. Identify the type of anemia associated with an increased risk of esophageal and oropharyngeal cancers.
9. Identify disorders causing abnormal vital signs and describe why the changes take place.
10. Differentiate between pernicious anemia and folic acid deficiency.
11. Describe what happens during a sickle cell crisis.
12. Describe the four major types of leukemia and identify the differences between them.

CHAPTER OUTLINE

The Hematopoietic System
Red Blood Cells
- Anemia
  - Hypochromic (iron deficiency) anemia
  - Plummer-Vinson syndrome
  - Thalassemia
  - Megaloblastic anemia
  - Sickle cell disease
- Anemia Associated with Chronic Diseases or Disorders
- Aplastic Anemia
- Polycythemia

White Blood Cells
- Neutropenia, agranulocytosis, cyclic neutropenia
- Lymphomas
  - Hodgkin lymphoma
  - Non-Hodgkin lymphoma
  - Burkitt lymphoma
  - Leukemia
  - Multiple myeloma

Hemostasis
- Bleeding disorders
- Thrombocytopenia
- Nonthrombocytopenic purpura

RELATED CLINICAL PROTOCOLS

#4 Treating Patients with Xerostomia
#19 Oral Health Care Management for the Patient with Cancer
#21 Oral Health Care Management for the Patient Taking Anticoagulant Medications

The Hematopoietic System

The **hematopoietic system** (blood cell–forming system) is composed of lymph tissue, bone marrow, and circulating blood. The thymus and bone marrow are considered to be the primary lymph organs. Other lymph tissues scattered throughout the body, such as the spleen, lymph nodes, the tonsils, appendix, and Peyer patches (organized aggregates of lymphoid tissue found in the intestine) are considered secondary lymph organs.

The thymus is the organ in which precursor immune system T cells mature into T cells that can recognize foreign antigens. The thymus attains its largest size about 1 year after birth. This size is maintained until just after puberty when the peripheral T cells have become established in lymph tissues throughout the body, and although the thymus continues to function, the gland begins to shrink in size. By the age of 50, the thymus consists largely of fatty tissue and may be only 15% of the size it once was.

Red and white blood cells are produced during a process known as **hematopoiesis,** which takes place in the red bone marrow. From birth until about the age of 4 years, all of the skeletal bones are packed with red marrow. After the age of 4, the growing size of the bones can accommodate far more red marrow than is necessary for replenishing the body's red and white blood cells; therefore, some of the red marrow is replaced with fatty tissues called yellow marrow. By adulthood, the red marrow is only found in the vertebrae, ribs, sternum, and ilia (hip bones). Yellow marrow can be reactivated to produce red and white blood cells if necessary. Reactivation may occur in disease states in which there is an increased need for red or white blood cells, such as anemia or leukemia, both of which are discussed later in this chapter.

The spleen comprises two functional areas: the red pulp is vascular and is responsible for trapping, destroying, and removing injured or senescent (old) red blood cells (RBCs), and the white pulp is packed with T cells, B cells, macrophages, and dendritic cells that filter and remove antigens from the body.

Lymph nodes and other lymphoid tissues are found throughout the body. Their functions are to remove foreign matter from the lymph before it enters the lymph vessels and to act as centers for the proliferation of immune system cells. See Chapter 4 for information on the function of the immune system.

The cells of the hematopoietic system are the red and white blood cells, and the interstitial space is the plasma. Blood distributes oxygen, nutrients, salts, and hormones to the cells and carries away the wastes from normal cellular metabolism. Blood also provides a line of defense against infection, toxic substances, and foreign antigens. **Erythrocytes,** or RBCs and platelets, are made in the red bone marrow. Leukocytes, or white blood cells, are made in the red marrow and lymph tissues. Erythrocytes, leukocytes, and platelets make up 45% of the blood, with plasma making up the remaining 55%. See Figure 9.1 for an illustration of hematopoiesis.

As seen in other types of systemic disorders, the first sign of a blood disorder may present in the oral cavity. Any unexplained change in the oral health of an individual should spark the interest of the dental professional. Signs that could indicate a systemic condition, including blood disorders, are as follows:

- Excessive or uncontrolled gingival bleeding
- Spontaneous gingival bleeding
- Unexplained petechiae, ecchymoses, or the tendency to bruise easily
- Pale mucosal tissues
- Glossitis and/or glossodynia (painful tongue)
- Nonhealing mucosal ulcers, recurrent fungal infections
- Exaggerated gingival response to local irritants such as dental biofilm (Wilkins, 2013)

Disorders of the hematopoietic system can be separated into three major groups: (1) diseases of erythrocytes (RBCs), (2) diseases of leukocytes (white blood cells), and (3) diseases of platelets.

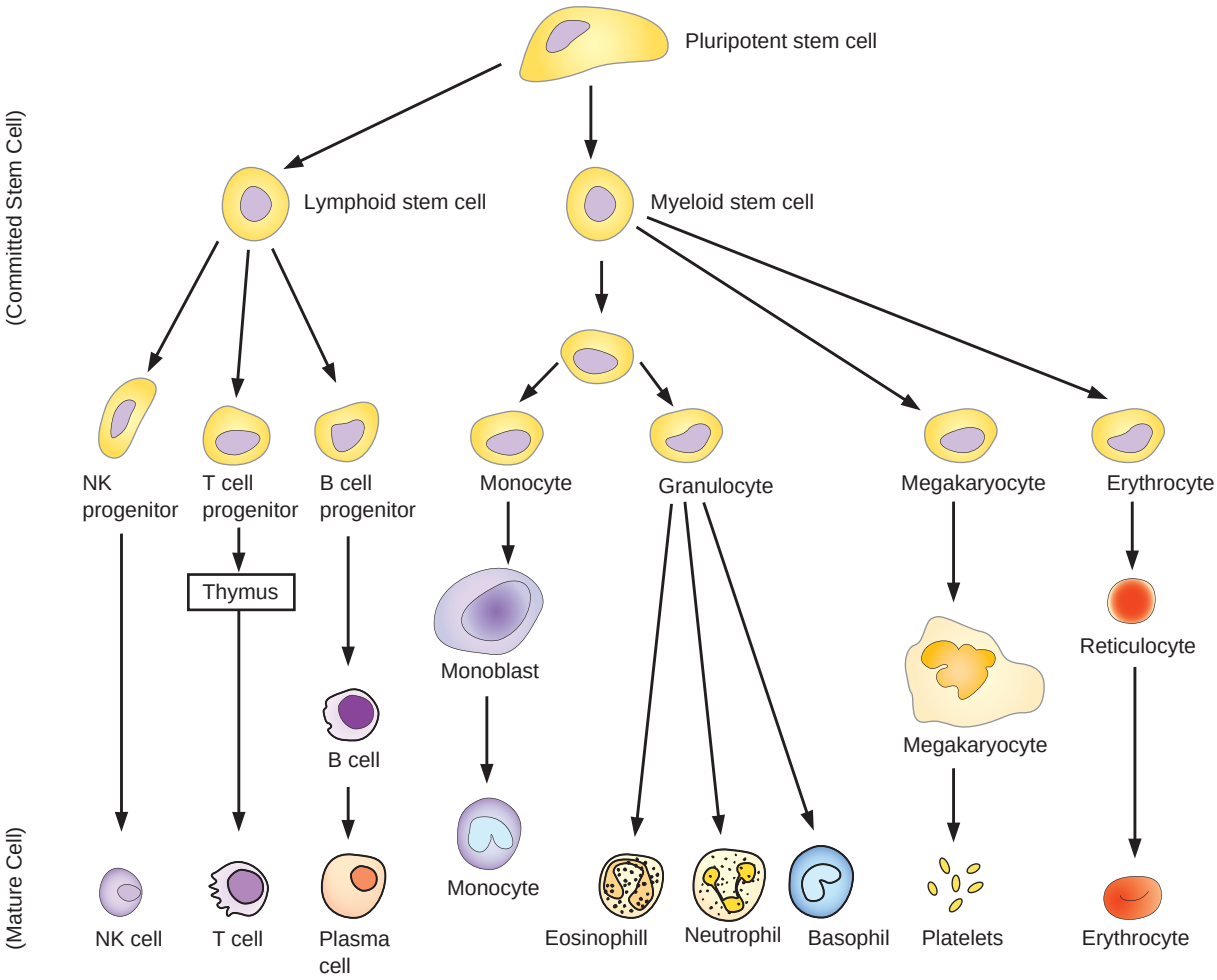

FIGURE 9.1. Hematopoiesis. Major developmental stages in the process of hematopoiesis. (From Porth CM. Essentials of pathophysiology: concepts of altered health states. 3rd ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins, 2011.)

Red Blood Cells

Approximately 1% of the body's RBCs are replaced each day, and each normal RBC has a life span of about 4 months, or 120 days. RBCs are formed in a process called **erythropoiesis**, which is regulated by the kidney through release of the hormone erythropoietin. Cells in the kidney sense low levels of oxygen in the circulating blood, which stimulates the production and release of erythropoietin, which in turn stimulates bone marrow to produce RBCs. RBC development occurs in the marrow of flat and long bones in children but only in the flat bones of the adult. See the illustration of RBC development in Figure 9.1. RBCs form from **pluripotential stem cells** (cells with the ability or potential to produce many different types of cells). RBCs are released from bone marrow as immature cells called reticulocytes. The reticulocyte takes about 24 hours to become a mature erythrocyte (Fig. 9.2). Blood disorders

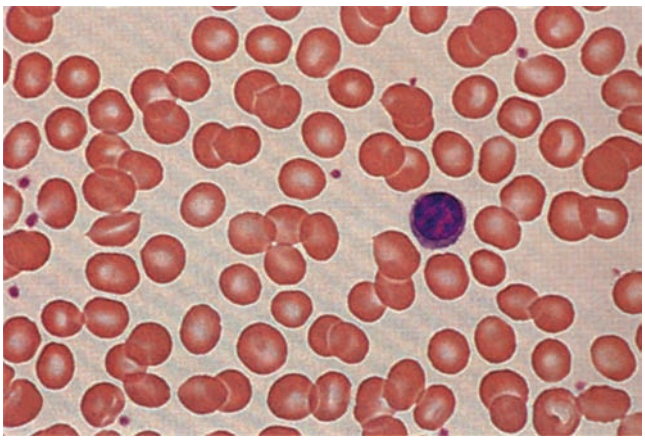

FIGURE 9.2. Erythrocyte. Scanning micrograph of normal red blood cells (RBCs) shows their characteristic concave appearance. (From Porth CM. Essentials of pathophysiology: concepts of altered health states. Philadelphia: Lippincott Williams & Wilkins, 2006.)

FIGURE 9.3. Jaundice. The yellow color of this individual's facial skin is compared with the skin color of an unaffected individual's hand. Note the sclera of the eye is also yellow. (From Smeltzer SC, Bare BG. Textbook of medical-surgical nursing, 9th ed. Philadelphia: Lippincott Williams & Wilkins, 2000.)

that cause the red marrow to create excessive numbers of RBCs can be detected by an increased number of circulating reticulocytes.

Approximately 1% of the body's RBCs are destroyed each day. This coincides with the number of RBCs normally produced every day. As red cells age, they become more fragile and have a tendency to rupture when traveling through the tiny vessels of tissues and organs. The damaged red cells are phagocytized by large mononuclear macrophages when they become trapped by the spleen. The body salvages and reuses most of the iron and amino acids from the destroyed cells, and the remaining waste is converted to bilirubin (a yellow substance). Bilirubin is transported to the liver and excreted in bile. When the liver is unable to remove bilirubin from the blood, because of either liver dysfunction or a condition that causes excessive destruction of RBCs, the yellow substance builds up in the tissues of the body, causing yellowing of the person's skin and mucous membranes, called **jaundice** (Fig. 9.3).

Diseases associated with RBCs can be separated into two categories: (1) anemia and (2) polycythemia.

Anemia

Anemia can be defined as a decrease in erythrocytes or in the amount, structure, or function of hemoglobin, the substance that carries oxygen to all the cells of the body. A decrease in the number of red cells can be due to excessive loss of blood, destruction of red cells, or decreased production of red cells by the bone marrow. An inadequate amount of hemoglobin is associated with insufficient dietary intake of iron and/or various genetic and acquired conditions that affect the production, function, or structure of hemoglobin.

The result of anemia, whatever its cause, is generalized tissue hypoxia. All forms of anemia share the classic clinical manifestations associated with the body's attempt to compensate for the inadequate level of oxygen in the tissues. The severity of the symptoms depends on the severity of the anemia. The individual experiences tachycardia and palpitations because the cardiovascular system compensates for anemia by increasing the heart rate in an attempt to get more blood, thus oxygen, to the tissues. The respiratory system responds by increasing rate and depth of respirations to bring more oxygen into the circulatory system, causing dyspnea (shortness of breath). The individual with anemia will experience dizziness and weakness and will fatigue easily. **Glossitis**, an inflamed sore tongue, is a common oral finding associated with many forms of anemia. Other clinical manifestations are specific for the type or cause of the anemia and are discussed in the following sections.

NAME: Hypochromic (iron deficiency) anemia

Etiology: Iron deficiency anemia is due to insufficient dietary intake, chronic blood loss, or an increased demand for iron, such as would occur during childhood or during pregnancy when there is a high rate of physical growth. Heavy menstruation, gastrointestinal ulcers, intestinal polyps, or hemorrhoids can cause chronic blood loss, depleting the body's iron stores and causing iron deficiency anemia.

Method of Transmission: Not applicable

Epidemiology: Iron deficiency anemia is the most common form of anemia worldwide; in the United States, it occurs more often in women of childbearing age than in any other age group.

Pathogenesis: Iron deficiency causes the production of microcytic (small) and hypochromic (pale) RBCs that do not carry the normal amount of oxygen. This creates a state of chronic hypoxia in which the body tries to increase the level of oxygen and compensate for a low level of oxygen at the same time. In addition to cardiac and respiratory compensatory mechanisms, the kidney releases increased levels of erythropoietin to stimulate the production of more RBCs that will also be deficient in iron and incapable of carrying sufficient oxygen. Thus the kidneys will continue to stimulate the marrow to produce RBCs. Most of the symptoms of iron deficiency anemia begin to manifest as more and more of the circulating red cells become immature reticulocytes.

Extraoral Characteristics: All of the classic signs of hypoxia including tachycardia, dyspnea, weakness, dizziness, and fatigue are present. The conjunctiva and exposed skin may appear pale. Long-term or chronic anemia may result in brittle hair and brittle, ridged, and concave or spoon-shaped fingernails. The patient's **hematocrit** (blood test determining the percentage of RBCs in whole blood) is lower than normal because of the small size of the erythrocytes. Table 9.1 summarizes the most common blood tests and normal values.

TABLE 9.1 **Common Blood Tests and Normal Values**

Name of Test	Explanation	Normal Range of Values
Hematocrit	Measures the red cell volume as a percentage of total blood volume	Male 42–52% Female 36–46%
Red blood cell (RBC) count	Measures the total number of RBCs/mm^3 of whole blood	Male 4.5–5.5 million/mm^3 Female 4.0–5.0 million/mm^3
Hemoglobin	Measures the total amount of hemoglobin in the blood, which reflects the number of erythrocytes	Male 14.0–17.0 g/dL Female 12.0–16.0 g/dL
Reticulocytes	Measures the total number of reticulocytes in the peripheral blood	18,000–158,000/mm^3 0.5–2.5% of erythrocytes
Platelets	Measures the total number of platelets in the blood	150,000–450,000 mcL
Leukocytes, total	Combined total of all types of white blood cells	4,500–11,000/mm^3
Neutrophils	Differential count, percentage of total	Band neutrophils 3–5% Segmented neutrophils 40–80%
Lymphocytes	Differential count, percentage of total	25–33%
Monocytes	Differential count, percentage of total	2–10%
Eosinophils	Differential count, percentage of total	0–5%
Basophils	Differential count, percentage of total	0–0.2%
Iron	Concentration in serum	Male 65–175 mcg/dL Female 50–170 mcg/dL

dL, deciliter; mm^3, cubic millimeter; mcg, microgram; mcL, microliter.

Perioral and Intraoral Characteristics: Mucosal membranes are pale. Generalized hypoxia slows the growth of epithelial tissues resulting in atrophy of oral soft tissues, causing glossitis (Fig. 9.4) and angular cheilitis, a tendency to form ulcers and other mucosal lesions, and burning sensations in the tongue and mucosa. Severe cases may present with difficulty swallowing, or dysphagia, due to the formation of a web of mucous and inflammatory cells in the oropharynx.

Distinguishing Characteristics: Glossitis, angular cheilitis, pale mucous membranes, and burning sensations in the tongue and mucosa should cause the dental professional to consider a systemic disorder such as anemia and prompt a medical referral.

FIGURE 9.4. Glossitis. Glossitis is a common oral finding in most types of anemia. Atrophy of the dorsal surface and loss of papillae produce a smooth, red and often sore tongue. (Courtesy of Cawson RA. From Cawson RA. Oral pathology. 1st ed. London, UK: Gower Medical Publishing, 1987.)

Significant Microscopic Features: The red cells in hypochromic anemia are microcytic and pale as seen in Figure 9.5.

Dental Implications: The patient with anemia may have abnormal pulse and respiration rates when vital signs are obtained prior to dental treatment. Review of the medical history may give some indication of the cause of symptoms associated with blood disorders. For example, the patient undergoing treatment for bleeding ulcers may have iron deficiency anemia due to chronic blood loss. Patients with anemia may become fatigued during dental treatment and may not be able to withstand long dental appointments. Individuals with untreated chronic iron deficiency anemia who exhibit dysphagia may have **Plummer-Vinson syndrome** (discussed below), which is associated with atrophy of the gastric mucosa and an increased risk of developing esophageal and oropharyngeal cancer. Patients who exhibit signs of anemia should be referred to their physician for a definitive diagnosis. Liquid iron administered orally may stain the teeth; this is avoided if the patient uses a straw to ingest the liquid.

Differential Diagnosis: Since different types of anemia share some common characteristics, all of the different forms of this condition need to be ruled out. Additionally, in the absence of general symptoms, the following oral conditions need to be investigated and ruled out:

1. Burning mouth syndrome, Chapter 10
2. Oral candidiasis, Chapters 13 and 14

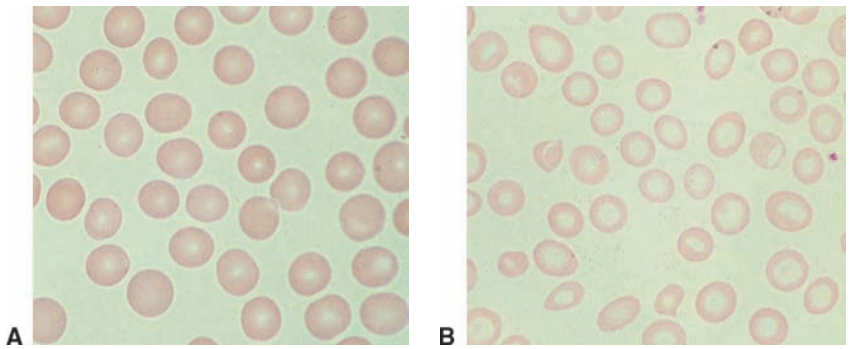

FIGURE 9.5. Hypochromic (iron deficiency) anemia. **A.** Normal erythrocytes with proper color, shape, and size. **B.** Microcytic–hypochromic (small, pale) erythrocytes in a patient with iron deficiency anemia. (From Willis MC. Medical terminology: a programmed learning approach to the language of health care. 2nd ed. Baltimore: Lippincott Williams & Wilkins, 2007.)

Treatment and Prognosis: Treatment for iron deficiency anemia focuses on providing adequate dietary iron and/or determining and eliminating the source of chronic blood loss. Symptoms associated with iron deficiency anemia begin to dissipate after about 1 to 2 weeks of oral iron supplementation and/or treatment/correction of disorders causing chronic blood loss. Supplementation is usually continued for 6 to 12 months. Untreated chronic iron deficiency anemia is associated with progressive cardiac dysfunction, increased potential for heart valve problems, and congestive heart failure.

Plummer-Vinson Syndrome (Paterson-Brown Kelly Syndrome)

Plummer-Vinson syndrome, or Paterson-Brown Kelly syndrome as it is known in the United Kingdom, is characterized by iron deficiency anemia associated with dysphagia caused by the presence of thin mucous membrane webs located in the upper esophagus. The esophageal webs partially obstruct the esophagus, causing difficulty swallowing. At present, this is a rare condition because of the improvement in nutritional status and decrease in iron deficiency in the world's population. It is seen in white women of about 40 to 60 years of age, but may be seen in children (Novacek, 2006). Plummer-Vinson syndrome is notable because it is associated with an increased risk of esophageal and oropharyngeal squamous cell carcinoma. Other manifestations indicating iron deficiency anemia may also be present, including pale mucous membranes, glossitis, angular cheilitis, and nail abnormalities (Novacek, 2006).

NAME: Thalassemia

Etiology: Thalassemia is caused by a genetically determined defect in the production of the hemoglobin molecule. There are several forms of hemoglobin; hemoglobin A, the most common adult hemoglobin, consists of two alpha (α)-polypeptide chains and two beta (β)-polypeptide chains. Figure 9.6 illustrates the structure of the hemoglobin A molecule. Other forms of hemoglobin are made up of these and other polypeptide chains. The two main types of this disorder are α-thalassemia, which is associated with a defect in the α chain, and β-thalassemia, which is associated with a defect in the β chain. There are many other types and subtypes in addition to the two main forms.

Method of Transmission: The thalassemias are caused by mutation or deletion of genetic material on the short arm (*p*) of chromosome 16 (α-thalassemia) and chromosome 11p (β-thalassemia). The amount and location of the deleted or changed material is what determines the type and severity of the disorder.

Epidemiology: The different forms of thalassemia as a group are the most common inherited disorders in the world. They are found in all ethnic groups and in every geographic area. The thalassemias are found more often in Mediterranean countries of Greece, Italy, and Spain; Southeast and Central Asia; India; the Middle and Far East; and Africa (Cao & Galanello, 2010; Galanello & Cao, 2011). The most severe forms of thalassemia are not common in the United States; however, the incidence of thalassemia types common in Asian populations is increasing rapidly in California and

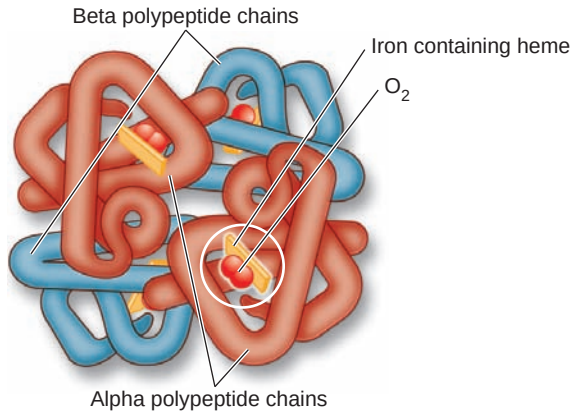

FIGURE 9.6. Hemoglobin A molecule. Each polypeptide chain is attached to a heme unit that contains an atom of iron. Each atom of iron can carry one molecule of oxygen; therefore, each molecule of hemoglobin can carry four molecules of oxygen (O_2) to the tissues of the body. (From McArdle WD, Katch FI, Katch VL. Essentials of exercise physiology. 2nd ed. Baltimore: Lippincott Williams and Wilkins, 2000.)

other West Coast states because of high numbers of Asian immigrants (Cheerva et al., 2011).

Pathogenesis: Defects in the α chain produce hemoglobin with such a high affinity for oxygen that it will not release it to the cells, thereby causing the severe hypoxia seen in α-thalassemia. In β-thalassemia, defective production of the β chain causes an inadequate production of hemoglobin that interferes with normal maturation of the red cell and contributes to its early destruction.

Extraoral Characteristics: Two pairs of genes are associated with α-thalassemia, and the clinical manifestations vary with the number of genes affected. The most severe manifestation, α-thalassemia major, is incompatible with life and occurs when all four genes associated with the production of the α chain of hemoglobin are affected. The deletion of one (silent carrier α-thalassemia), two (α-thalassemia trait), or even three (Hb H disease) of the associated genes results in a full range of classic symptoms associated with anemia from none to mild or moderate signs of anemia, respectively.

β-Thalassemia occurs in three clinical forms: β-thalassemia minor, β-thalassemia intermedia, and β-thalassemia major. Most individuals with the minor form of the disorder do not have classic symptoms of anemia unless they have a contributing factor, such as inadequate dietary intake of iron or chronic blood loss due to an ulcer, for example. In these instances, the person with β-thalassemia minor would be less able to compensate for these factors and would develop signs and classic symptoms of anemia sooner than someone without the disorder. Individuals with β-thalassemia intermedia have mild-to-moderate signs of anemia, and individuals with β-thalassemia major have severe anemia that must be treated with transfusions. Those affected by β-thalassemia major exhibit bony malformations and stunted growth due to the expansion of the bone marrow as it tries to create more and more red cells, and jaundice because of the increased destruction of RBCs.

Perioral and Intraoral Characteristics: Patients with β-thalassemia minor and intermedia and the lesser forms of α-thalassemia may exhibit no oral abnormalities other than possible pallor of the oral soft tissues. β-Thalassemia major may cause changes in the trabecular pattern of the oral and cranial bones. The jaw bones may appear more radiolucent and have a honeycomb trabecular pattern, while the radiologic appearance of the surface of the skull may exhibit the "hair-on-end" effect, characteristic of β-thalassemia major (Fig. 9.7). The zygoma and maxilla will be more prominent (Fig. 9.8), and there may be abnormal spacing and flaring of the maxillary incisors. The laminar dura may be thin or absent in some areas. Bossing (protuberance) of the frontal bone is likely.

Distinguishing Characteristics: The craniofacial abnormalities seen in β-thalassemia major along with appropriate laboratory test results distinguish this from other forms of this disorder and from other anemias.

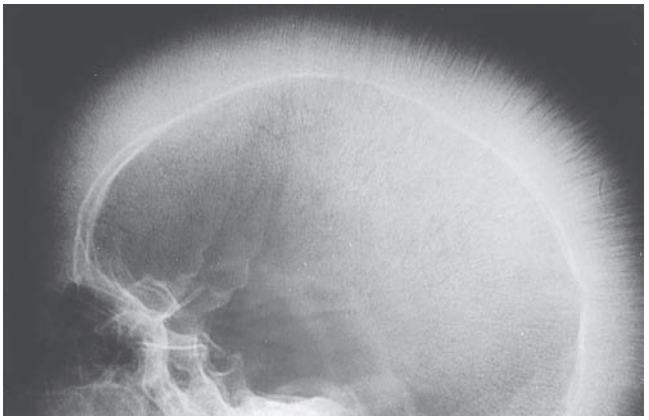

FIGURE 9.7. Thalassemia. The "hair-on-end" effect occurs when the space between inner and outer bone layers of the cranium expands in order to allow the marrow to produce more RBCs. The bone trabeculae within the space then become oriented in a direction that is perpendicular to the layers of the bone. (From Yochum TR, Rowe LJ. Yochum and Rowe's essentials of skeletal radiology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 2004.)

FIGURE 9.8. β-Thalassemia major. A patient with β-thalassemia major demonstrates the characteristic facial appearance of a prominent maxilla with flaring of the anterior teeth. (Courtesy of Dr. Faiez N. Hattab.)

Significant Microscopic Features: The red cells produced in thalassemia are microcytic and hypochromic.

Dental Implications: Individuals who have had their spleen removed because of severe enlargement need to be evaluated for prophylactic antibiotics prior to dental/dental hygiene care. In addition, these individuals may be on anticoagulant therapy, and their coagulation status should be determined prior to therapy. Annual orthodontic evaluations should be done during childhood because of the tendency for occlusion problems associated with an increased overjet, spacing of maxillary teeth, and delayed eruption of primary and permanent teeth (Hazza'a & Al-Jamal, 2006).

Differential Diagnosis: Not applicable

Treatment and Prognosis: There is no definitive treatment for the thalassemias because of the genetic etiology; however, genetic engineering may hold some promise for the future. Individuals with minor forms of thalassemia usually require little, if any, treatment. β-thalassemia major requires routine transfusions to manage the symptoms of the disease. The average life expectancy is decreased for those with β-thalassemia major because of complications associated with chronic anemia such as heart failure and the chronic iron overload associated with frequent transfusions. Stem cell transplantation has shown some promise for treating this disease, especially in low-risk young patients where it has had excellent results (Porth, 2011).

NAME: Megaloblastic anemia

Etiology: Megaloblastic anemia is characterized by abnormally large erythrocytes that are the result of defective deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) synthesis. The most common causes of megaloblastic anemia are vitamin B_{12} deficiency and folic acid deficiency.

One of the major causes of vitamin B_{12} deficiency is **pernicious anemia,** an autoimmune condition that is characterized by the inability of the gastric mucosa to produce intrinsic factor (IF). IF is necessary for the transportation of vitamin B_{12} across the intestinal mucosa. If there is no IF, there is no absorption of vitamin B_{12}. Vitamin B_{12} deficiency can also result from inadequate dietary intake, malabsorption syndromes (Chapter 10), alcoholism, and pancreatic disorders, and rarely, in individuals adhering to strict vegetarian diets.

Folic acid deficiency is usually due to inadequate intake or an increased requirement resulting in inadequate intake of folic acid. However, it can also be due to impaired absorption associated with malabsorption syndromes (Chapter 10), impaired metabolism associated with alcoholism, or the existence of neoplastic disease, which increases the need for folic acid because of the uncontrolled growth of cells.

Method of Transmission: The deficiency states are not transmissible. However, the inability of the stomach to produce IF seen in pernicious anemia appears to have a genetic component linked to mutations on chromosomes 10p and 14q (OMIM, 2011a,b).

Epidemiology: In the United States, pernicious anemia occurs in about 10 to 20 out of 100,000 individuals. It usually occurs in those over the age of 60. It is more common in people of northern European descent but is found in all races (Schick & Conrad, 2011).

Children and adolescents have a higher requirement for folic acid because of the demands that growth places on the body. Pregnant women require higher levels of folic acid and thus are more apt to be deficient. The elderly have a higher risk of folic acid deficiency, not because of growth requirements, but because of dietary choices and socioeconomic status. Women between the ages of 20 and 40 are the most likely to be deficient in folic acid, which, of course, parallels the reproductive years (Gentili et al., 2011).

Pathogenesis: Vitamin B_{12} and folic acid are both essential for the synthesis of DNA and RNA. Defective DNA and RNA synthesis causes delayed maturation of the nucleus of the RBC, while the cytoplasm matures normally, producing the large cells seen in this type of anemia. In addition to the large size of the erythrocytes, they are more oval in shape and have a thinner-than-normal cell membrane, which increases the likelihood of rupture. These cells have a short life span of several weeks as opposed to the norm of several months, requiring the individual to produce more red cells than normal, which results in anemia. Vitamin B_{12} is also necessary for the maintenance of the myelin sheaths covering neurons. Without vitamin B_{12}, there is a tendency for the myelin sheaths to break down, resulting in central and peripheral nervous system dysfunction.

Extraoral Characteristics: The symptoms associated with RBC abnormalities are the same for both vitamin B_{12} and folic acid deficiency. The generic symptoms of anemia are present, including fatigue, dyspnea, and tachycardia. Darker-skinned individuals may present with blotchy skin pigmentation, and lighter-skinned individuals may have a lemon yellow, jaundiced appearance. In addition, chronic vitamin B_{12} deficiency will cause neurologic symptoms such as paresthesia of the hands and feet, loss of **proprioceptive** ability (the ability of a person to be aware of the position of their body), and **ataxia** (jerky uncoordinated movements). Neural tube birth defects have been linked to folic acid deficiency. Recent studies have shown that 50% and more of neural tube defects (NTDs), such as spina bifida, may be prevented by an adequate dietary intake of folic acid by the mother prior to, and during, pregnancy (Blom et al., 2006).

Perioral and Intraoral Characteristics: Oral mucous membranes may be pale and ulcerated, with the tongue appearing smooth, "beefy red," and sore, due to atrophy of the papillae. Along with NTDs, there is evidence to support a link between folic acid deficiency and the development of cleft lip and/or palate.

Distinguishing Characteristics: Vitamin B_{12} deficiency can be differentiated from folic acid deficiency in severe cases because of the additional manifestation of neurologic symptoms; otherwise, there is no difference between the two entities.

Significant Microscopic Features: Megaloblastic erythrocytes are abnormally shaped but have normal hemoglobin concentrations (Fig. 9.9).

Dental Implications: As in iron deficiency anemia, vital signs may be abnormal, and the patient may fatigue easily. These patients should be referred to their physician for evaluation. Provide patient education about the need for adequate levels of folic acid to help prevent cleft lip and palate. See Application 9.1.

Differential Diagnosis: It is important to determine if the cause is vitamin B_{12} or folic acid deficiency because treating a B_{12} deficiency as if it is a folic acid deficiency can lead to permanent neurological damage. Additionally, in the absence of general symptoms, the following oral conditions need to be investigated and ruled out:

1. Burning mouth syndrome, Chapter 10
2. Oral candidiasis, Chapter 14

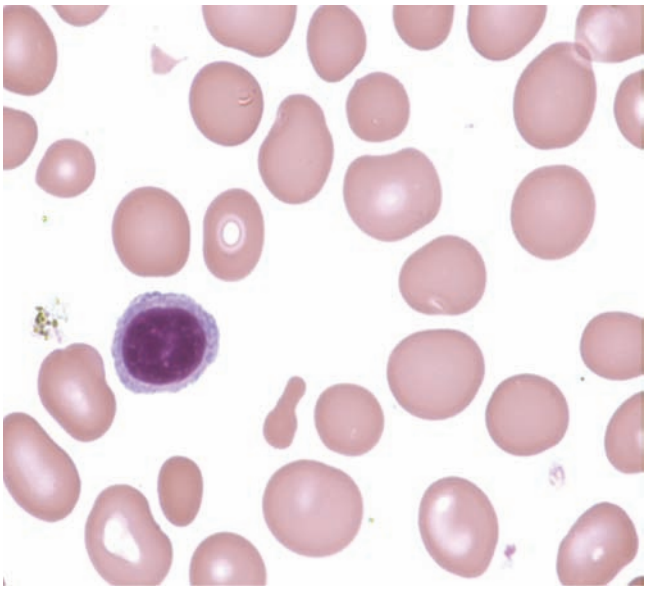

FIGURE 9.9. Megaloblastic anemia. In this smear of blood from a patient with folic acid deficiency, the erythrocytes are large and often oval as compared with normal erythrocytes as shown in Figure 9.5A. (From Anderson SC. Anderson's atlas of hematology. Baltimore: Wolters Kluwer Health/Lippincott Williams & Wilkins, 2003.)

APPLICATION **9.1**

Folic Acid and Birth Defects: An Educational Opportunity

Neural tube defects (NTDs) such as spina bifida are among the most devastating birth defects involving the central nervous system seen today. Worldwide, approximately 300,000 children are born with these defects each year with about 3,000 born in the United States annually (Dunlap et al., 2011). Most of these defects are thought to have a multifactorial etiology including genetic as well as environmental elements. Research focusing on finding methods to prevent or decrease the risk of these defects has found a significant relationship between low or deficient levels of folic acid and an increased risk of having a child born with an NTD. Folic acid supplementation has been shown to reduce NTDs by 53% and more, a highly significant reduction (Dunlap et al., 2011). Since 1992, public health awareness campaigns have passed this message along to women using a variety of means; however, a survey done in 1997 showed only 6% of women of childbearing age actually knew they should begin taking folic acid prior to becoming pregnant (Green-Raleigh et al., 2006). In 1996, the Food and Drug Administration (FDA) recommended fortifying certain grains with folic acid, and in 1998, the United States became the first country to mandate fortifying enriched grains (flour, bread, cornmeal, rice and pasta, among others) with 140 mg of folate per 100 g of flour. By 2008, 67 countries had followed the United States by fortifying wheat flour with varying amounts of folic acid. Nevertheless, in the United States, most nonpregnant women still do not get the recommended daily allowance of 0.4 mg. Most physicians recommend that their pregnant patients take vitamin supplements including folic acid; patients often do not follow their advice. Factors predicting low use of supplements include young age, single, history of unplanned pregnancy, immigrant, non-White race, low educational level, and low socioeconomic status (Dunlap et al., 2011). In addition, 86% of women in a 2005 survey reported they would have taken a supplement if they had been advised by their health care provider, but only 26% said their health care provider told them about folic acid and its benefits (Green-Raleigh et al., 2006).

There has been much discussion about whether folic acid can also play a role in preventing orofacial clefts (OFCs) such as cleft lip and/or palate. While the evidence for preventing NTDs is relatively strong, there is mixed evidence surrounding the use of folic acid to prevent OFCs. The available evidence "suggests" folic acid may very well play a role in the prevention of OFCs. More research focused on OFCs rather than NTDs needs to be done in order to provide a reliable evidence base for any decisions or recommendations regarding the use of folic acid to prevent OFCs (Wehby & Murry, 2010; Fernandez-Gaxiola et al., 2010).

The evidence supporting reduced risk of NTDs with appropriate levels of folic acid is strong, and the dental hygienist is in an excellent position to educate women of childbearing age about the benefits of folic acid supplements in preventing NTDs and the suggested link between folic acid and preventing OFCs. The current recommendations for supplementation are as follows: women of childbearing age should be taking 0.4 mg of folic on a daily basis to prevent NTDs and women who have had one child with an NTD or are at high risk should be taking 4.0 mg of folic acid per day (Dunlap et al., 2011). For more information, visit the Web sites listed below.

CDC Folic Acid Web Site: http://www.cdc.gov/ncbddd/folicacid/index.html

National Council on Folic Acid: http://folicacidinfo.org/

Treatment and Prognosis: Treatment for folic acid deficiency anemia focuses on replacing folic acid in the individual's diet. The prognosis for treated individuals is excellent because dietary folic acid replacements rapidly eliminate the symptoms of this disorder.

Vitamin B_{12} deficiency is slightly more complex to treat because the reason for the deficiency has to be determined first. If the deficiency is due to an inadequate intake of vitamin B_{12} in the diet, the treatment is to increase the intake until normal blood levels are achieved. If the cause of the deficiency is lack of IF or pernicious anemia, treatment will be lifelong administration of intramuscular injections of vitamin B_{12}, since dietary B_{12} cannot pass across the gastric mucosa. The prognosis is excellent when individuals who have vitamin B_{12} deficiency are treated adequately. However, if left untreated, neurologic symptoms associated with the deficiency may become permanent (Schick, 2011).

NAME: Sickle cell disease

Etiology: Sickle cell disease (SCD) (anemia) is one of a group of inherited disorders that result in the creation of abnormal hemoglobin. The abnormality is caused by the substitution of the amino acid valine for glutamic acid at the sixth position in the hemoglobin β chain. SCD is considered a **hemolytic** anemia because the anemia is caused by the destruction or lysis of the abnormal RBCs.

Method of Transmission: SCD follows an autosomal recessive inheritance pattern. Heterozygous individuals (with one normal and one defective gene) are said to have sickle cell trait. The genetic abnormality is found on the short arm of chromosome 11 and involves the same genetic material associated with β-thalassemia.

Epidemiology: SCD is the most common inherited blood disorder in the United States, occurring in about 1 of every 500 black newborns. Approximately 8% of blacks carry the sickle cell trait. SCD is also seen in Mediterranean, Middle Eastern, and Indian population groups. Males and females are equally affected (Maakaron et al., 2012).

Pathogenesis: Hemoglobin that forms as a result of the genetic mutation is called hemoglobin S, or HbS. HbS reacts to low levels of oxygen or dehydration by combining with adjacent HbS molecules and forming a larger solidified mass, which causes the erythrocyte to stretch into the long sickle shape characteristic of RBCs in this disease (Fig. 9.10). The abnormal cells cause hemolytic anemia and occlusion of blood vessels. RBCs in a person with SCD have only a 20-day life expectancy as opposed to the normal 120 days, resulting in a chronic state of anemia from decreased numbers of red cells. The abnormally shaped cells tend to get caught in the microvasculature or capillaries because they are not as flexible as normal RBCs, which are able to deform and squeeze through tight areas. As more and more cells are trapped in an area, they form aggregates or clots within the microvasculature, causing ischemia or infarcts in the areas distal to them. These thrombi can form in any tissue or organ, causing severe pain and possible necrosis of the tissues.

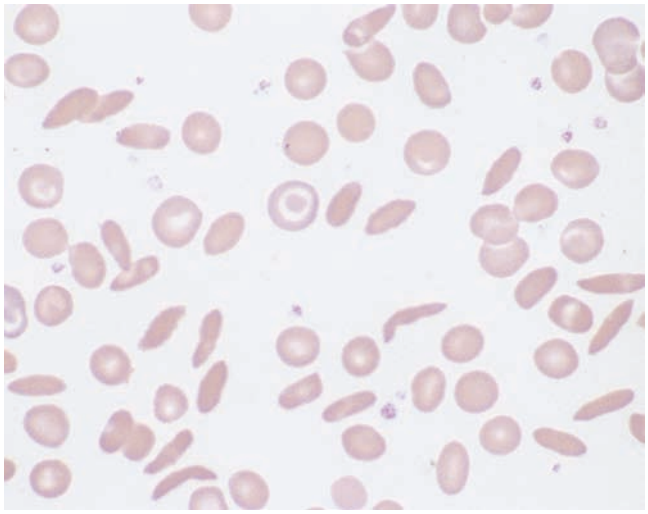

FIGURE 9.10. Sickle cell anemia. Note the sickled shape of some of the cells in this blood smear. RBCs can become permanently sickled after repeated events. (From McKenzie SB, Clare N, Burns C, et al. Textbook of hematology. 2nd ed. Baltimore: Williams & Wilkins, 1996.)

Sickle cell crises are episodic exacerbations brought on by cold, stress, physical exertion, dehydration, acidosis, infectious agents, and above all, hypoxia or a low level of oxygen. During a crisis, there is sickling of many RBCs, which occlude the microvasculature in many areas, such as the chest, abdomen, and bones, causing extreme pain.

Extraoral Characteristics: Individuals with SCD exhibit all of the symptoms of chronic severe anemia. Jaundice may also be present, since this is a hemolytic condition. Sickle cell anemia causes damage in almost every organ in the body. See Table 9.2 for a description of the most common complications related to this condition. Chronic pain is often a debilitating factor for these patients and many suffer from psychologic problems such as depression as a result.

Perioral and Intraoral Characteristics: There are no specific oral manifestations of SCD other than possible bone pattern changes noted in radiographs. "Hair-on-end" spicules may be seen on the surface of the skull similar to that seen in thalassemia and a "stepladder" trabecular pattern may be observed between adjacent posterior teeth (Fig. 9.11).

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: The elongated sickle shape of the RBCs is characteristic of this disease.

Dental Implications: Dental care focuses on preventing any dental infections that might trigger a crisis. Education is extremely important for the individual or family and should be the anchor for a consistent oral care provider

TABLE 9.2 **Complications of Sickle Cell Anemia**

Organ	Disorder	Cause(s)
Heart	Enlarged heart	Increased work necessary in any chronic anemia
	Congestive heart failure	Due to constant cardiac overload
	Coronary artery obstructions	Thrombus formation from aggregated or clotted sickled cells
Lungs	Acute chest syndrome	Pneumonia associated with lung infarcts
Spleen	Enlarged spleen	Due to the removal of excessive numbers of sickled cells from the circulation
	Fibrosis of the spleen	Chronic damage due to slow blood flow
Brain	Transient ischemic attacks	Thrombus formation from aggregated or clotted sickled cells
	Stroke	Thrombus formation from aggregated or clotted sickled cells
	Hemorrhage	Thrombus formation from aggregated or clotted sickled cells
Kidney	Renal infarcts	Thrombus formation from aggregated or clotted sickled cells
Gall bladder	Gallstones	High levels of bilirubin
	Cholecystitis	Inflammation of the gall bladder due to gallstones
Skin	Ulcers	Obstruction of the cutaneous capillaries resulting in ischemia and necrosis of the tissues
Bones	Aseptic necrosis, especially of the femoral head	Thrombus formation from aggregated or clotted sickled cells
	Osteomyelitis	Infection of the bones in areas of ischemia
Eyes	Retinal hemorrhage	Thrombus formation from aggregated or clotted sickled cells
	Retinal detachment	Thrombus formation from aggregated or clotted sickled cells
	Blindness	Thrombus formation from aggregated or clotted sickled cells

relationship with the patient. Short appointments, stress reduction, and the use of local anesthetics with little or no vasoconstrictors should be considered when treating these patients. Poor wound healing can be expected because of the severe chronic anemia. Thus, unnecessary oral trauma during treatment should be avoided. Supplemental oxygen might be used to control the blood oxygen level and avoid the hypoxia that could trigger a crisis. Prophylactic antibiotic coverage may be necessary for surgical procedures such as tooth extraction or periodontal surgery (Ramakrishna, 2007).

FIGURE 9.11. Sickle cell anemia. Periapical radiograph showing widely spaced, "stepladder" trabecular pattern. (Courtesy of Dr. Mel Mupparapu.)

Differential Diagnosis: Not applicable

Treatment and Prognosis: There is no definitive treatment for sickle cell anemia because it is an inherited disorder; however, there are ways to manage the disease. Treatment includes pain control, maintaining adequate hydration and oxygenation, and managing the complications of the disease. Affected individuals need to avoid situations exposing them to cold, stress, physical exertion, dehydration, acidosis, and infectious agents. Transfusions may be necessary in cases of severe disease or crisis.

Mortality is high in early childhood and many do not live beyond 20 years, but life expectancy appears to be improving slightly (Maakaron et al., 2012). Stem cell transplants are becoming a treatment option for childhood sickle cell anemia and offer a "cure" if they are successful; however, there is a very high risk of graft versus host disease and subsequent failure of the procedure. Gene therapy is also being tested with success in lab animals, and human trials are being considered in the very near future.

Individuals with sickle cell trait very rarely suffer any symptoms of the disease and then only under conditions of extreme hypoxia or dehydration. These individuals have a normal life expectancy. It is well known that individuals with sickle cell trait are less susceptible to malaria than individuals who do not carry the trait. This can be explained by the fact that when the malaria organism enters a RBC, it actually triggers the cell to become sickled. The sickle cell is then trapped in the spleen and destroyed, along with the malaria organism living within it.

TABLE 9.3 Chronic Conditions Associated with a Secondary Anemia

Primary Condition	Type of Anemia	Cause
Cancer	Iron deficiency	Rapidly reproducing neoplastic cells compete for the available iron
Chronic inflammatory diseases (rheumatoid arthritis, systemic lupus)	Iron deficiency	Inflammatory mediators are believed to interfere with the metabolism of iron
Renal disease	Low RBC count	Decreased release of erythropoietin by the kidneys
Hypertension	Hemolytic	Mechanical destruction of the cells due to the high pressure under which they are moved through the vessels
Prosthetic heart valves	Hemolytic	Mechanical destruction as they move through the replaced valve
Turbulent blood flow	Hemolytic	Mechanical destruction caused by trauma to the red cells as they move through areas of turbulent blood flow

Anemia Associated with Chronic Diseases or Disorders

Anemia is often seen as a complication of other conditions. Treatment of these conditions may eliminate the anemia; if not, supportive measures to increase the production of red cells is indicated to manage the disorder. Refer to Table 9.3 for a listing of conditions that may present with anemia as a comorbid (coexisting but unrelated) condition.

Aplastic Anemia

Aplastic anemia occurs when the bone marrow fails to produce any of the three types of blood cells. The underlying cause is destruction or injury to the pluripotential stem cells from which all cellular elements of the blood originate. Eighty percent of all cases are acquired (linked to various chemical, microbial, and environmental agents); the other 20% are mostly congenital or inherited (Bakhshi, 2011) (see Box 9.1).

Whatever the cause, the bone marrow stops, or drastically reduces, production of all of the cellular components of blood. As the disease progresses, the bone marrow is replaced with fatty tissue. The general symptoms of anemia are accompanied by increased bleeding tendencies, due to decreased platelet levels, and an increased chance of infection, due to the decreased white blood cell level. Severe periodontal and gingival infections may be present, along with severe and/or spontaneous gingival bleeding. Oral mucosal tissues may exhibit multiple petechiae and ecchymoses due to bleeding within the oral epithelium. Epistaxis is also common.

BOX 9.1 Etiologic Agents Associated with Aplastic Anemia

- **Acquired**
  - Chemicals/Drugs
    - Chloramphenicol
    - Phenylbutazone
    - Gold
    - Antineoplastic chemotherapeutic agents
    - Benzene
  - Environment
    - Ionizing radiation
  - Microbes
    - Hepatitis viruses
    - Epstein-Barr virus
    - Parvovirus
    - HIV
    - Mycobacteria
  - Conditions
    - Graft versus host disease associated with transfusions
    - Pregnancy
    - Malignancies
- **Congenital/Inherited**
  - Fanconi anemia
  - Other disorders presenting with bone marrow failure

Treatment focuses on identifying and removing the cause of the anemia when possible. Otherwise, therapy includes bone marrow transplantation and immunosuppressive therapy for those who are not candidates for bone marrow transplant. Untreated aplastic anemia is fatal.

Polycythemia

Polycythemia is the opposite of anemia. Polycythemia refers to an excess of RBCs in relationship to plasma or a hematocrit over 50%. The increase in volume of blood cells causes an increase in the viscosity of the blood, which can impair blood flow to the extremities and increase the tendency to form thrombi. Polycythemia can be further defined by the following categories: relative, primary, and secondary.

Relative polycythemia occurs when a decrease in plasma fluid is the cause of the increased ratio of RBCs to plasma. The most common cause of relative polycythemia is dehydration, resulting from inadequate water intake or excessive output, as occurs in diarrhea or the use of diuretics. Treatment for relative polycythemia focuses on replacing the fluid volume, determining the cause of the dehydration, and treating the underlying problem.

Primary polycythemia, or polycythemia vera, occurs when there is an increase in all types of formed blood products, caused by a proliferative neoplastic disease. This rare disorder usually occurs between 50 and 70 years

FIGURE 9.12. Polycythemia vera. The arm of the patient with polycythemia appears much redder and engorged or swollen as opposed to an unaffected person's arm. ("Erythromelalgia," © Herbert L, Fred MD, Hendrik A. van Dijk, used under a Creative Commons Attribution license (CC-BY 2.0): http://creativecommons.org/licenses/by/2.0/)

of age. The clinical manifestations are due to the increase in blood volume associated with this disease and include intense reddening of the skin and mucous membranes, swelling, increased blood pressure, headaches, visual disturbances, Raynaud phenomenon, intense pruritus, and **hypercoagulation** (overproduction of clots) (Fig. 9.12). Complications from this disorder include thrombus and embolus formation and the resultant infarcts and hemorrhage they produce. Polycythemia vera is treated with regular **phlebotomy** (bloodletting) to decrease the absolute amount of circulating blood. Other treatments include radioactive destruction of some of the bone marrow and myelosuppressive drug therapy, which decrease the production of cells within the bone marrow. Untreated, the disease will cause death within 1 to 3 years of the onset of symptoms; recent therapeutic and preventive advances have increased survival time by 10 to 20 years and more (Besa & Woermann, 2012).

Secondary polycythemia, sometimes called erythrocytosis, refers to a condition in which only the red cells are increased. Secondary polycythemia occurs in response to chronic tissue hypoxia due to pulmonary disorders, cardiovascular disorders, smoking, living at high altitudes where ambient oxygen levels are low, and engaging in sports requiring constant strenuous activity, such as marathon running. Tissue hypoxia stimulates the kidney to release erythropoietin, which in turn stimulates the bone marrow to produce more red cells. When there are enough red cells to eliminate tissue hypoxia, release of erythropoietin will cease and so will production of red cells. This is one reason athletes will travel several weeks early to a sport venue located at a higher altitude then they are used to so they can build up RBCs to accommodate the change in ambient oxygen at the higher altitude (Application 9.2).

White Blood Cells

Like the other cellular components of blood, white blood cells or leukocytes are formed within the bone marrow from the same pluripotential stem cells that form erythrocytes. Differentiation results in the formation of a lymphoid stem cell that develops into lymphocytes and a myeloid stem cell that develops into monocytes, granulocytes, platelets, and erythrocytes. Figure 3.5 in Chapter 3 illustrates the major types of white blood cells. The following sections focus on disorders of the granulocytes, monocytes, and lymphocytes. See Figure 9.1 for an illustration of hematopoiesis.

NAME: Neutropenia, agranulocytosis, cyclic neutropenia

Etiology: Neutropenia is defined as a low neutrophil count, less than 1,500 cells per microliter (μL) of blood (Porth, 2011). Agranulocytosis usually refers to the virtual absence of neutrophils. For the purpose of this discussion, all inadequate neutrophil levels are called neutropenia. The most common cause of neutropenia is either an idiosyncratic or adverse reaction to a drug. Other causes include inherited syndromes, overwhelming viral or bacterial infections, autoimmune destruction of the neutrophils, bone marrow neoplasms, and anemia. Transient neutropenia is an expected side effect of almost all of the chemotherapeutic agents used to treat cancer. Cyclic neutropenia is an autosomal dominant disorder characterized by recurring episodes of neutropenia (approximately every 21 days) that last 2 to 3 days.

Method of Transmission: Inherited forms follow various inheritance patterns including the autosomal dominant cyclic neutropenia. Neutropenia resulting from infectious agents is not transmitted by the microbes but is rather a reaction to the infection itself.

APPLICATION **9.2**

High-Altitude Energy

A simple experiment can illustrate the phenomenon that occurs at high altitudes. The next time you take a trip from sea level to a higher altitude, be aware of the length of time it takes you to become accustomed to the high altitude and lower ambient oxygen level. The experimental aspect begins when you return home or at least to a much lower altitude and try to jog a few miles. You will find you have more energy and stamina than you ever thought possible. In fact, you will probably be motivated to attempt it again the next day. However, it is very likely your next day's experience will not be anywhere near as satisfying as the previous day's because the effects of erythrocytosis have already dissipated. This occurs because of the normal daily destruction of red cells and the fact tissue hypoxia is not present to stimulate the production of more red cells. Good luck with your experiment!

Epidemiology: The exact frequency of neutropenia is unknown. It occurs slightly more frequently in women than in men, and it occurs in all age groups (Godwin et al., 2011).

Pathogenesis: The absolute number of circulating neutrophils is decreased because of decreased production, production of defective cells, increased destruction, or removal of cells from the circulation. The major effect is an increased susceptibility to infections. Individuals are usually asymptomatic until the neutrophil count approaches 500 cells/μL.

Extraoral Characteristics: Individuals with neutropenia present with fatigue, fever, malaise, and extreme weakness. Vital signs may show a rapid pulse, increased respirations, and hypotension due to septic shock (a condition that causes dilation of peripheral blood vessels). They may have obvious signs of skin infections, but without the purulent exudate and erythema that would accompany a cellular immune response. Upper respiratory and genitourinary tract infections are very common and are usually caused by microorganisms that normally inhabit the body without being pathogenic.

Perioral and Intraoral Characteristics: Oral infections are common and very severe. Periodontal disease is very aggressive and painful. Chronic neutropenia and the cyclic form of neutropenia invariably lead to premature loss of the dentition. Oral ulcers are common with this condition and can impair the individual's ability to maintain adequate nutrition and hydration (Fig. 9.13).

Distinguishing Characteristics: Rapid, progressive loss of periodontal attachment indicates this disorder as well as other disorders that affect the number of white blood cells available to fight infection. Cyclic neutropenia is distinguished by recurrent decreases in white blood cells followed by a return to normal levels.

FIGURE 9.13. Neutropenia. Transient neutropenia caused by chemotherapy can cause gingival infections and ulceration as seen in this photo. (From Fleisher GR, Ludwig S, Baskin MN. Atlas of pediatric emergency medicine. Philadelphia: Lippincott Williams & Wilkins, 2004.)

Dental Implications: Dental care for individuals with neutropenia focuses on preventing infections and preserving the dentition. Patient education related to oral infection control and biofilm removal is very important. Preventing oral infections is not only crucial in preserving the dentition, but it plays a key role in decreasing the chance of a systemic infection as well. Appropriate medical consultation and laboratory tests should be obtained, since dental treatment should not be performed unless neutrophil levels are adequate (Pickett & Gurenlian, 2010).

Differential Diagnosis: Any disorder that presents with severe periodontal infections should be ruled out, including the following:

1. Papillon-Lefèvre syndrome, Chapter 6
2. Leukemia, Chapter 9
3. Diabetes-associated periodontal disease, Chapter 7

Treatment and Prognosis: Treatment focuses on using antibiotics to prevent infections and boosting the production of neutrophils by administering drugs containing *colony-stimulating factor*. This factor stimulates the precursor cells in the bone marrow to produce more neutrophils, thereby accelerating their maturation and releasing them into the circulation. The prognosis for neutropenia depends on the type, cause, and severity of the disorder. Untreated neutropenia usually results in death from infection. Most forms of neutropenia have an excellent prognosis once the condition is identified and the etiologic agent removed; recovery may be complete. Neutropenia caused by cancer chemotherapy is eliminated once treatments are completed.

Lymphoma

The term "lymphoma" represents a heterogeneous group of malignancies involving the lymphocyte. Hodgkin lymphoma, a malignancy involving an atypical form of B cell, is discussed separately from the other forms of lymphoma (non-Hodgkin lymphomas) because of its distinctive cellular morphology and disease manifestations. Non-Hodgkin lymphomas include neoplasms associated with B cells, T cells, and natural killer cells.

NAME: Hodgkin lymphoma (Hodgkin disease)

Etiology: The etiology of Hodgkin lymphoma is unknown, but several risk factors exist. Infection with the Epstein-Barr virus (EBV), conditions that cause immunosuppression, such as infection with human immunodeficiency virus (HIV), and genetic factors have been tentatively identified by researchers (ACS, 2011). Almost 100% of Hodgkin lymphoma cases seen in individuals infected with HIV are EBV positive (Dessain et al., 2011). Genetic predisposition is suggested because siblings of an affected individual have a three- to seven-fold greater risk for developing the disease than those without this connection (Dessain et al., 2011).

Method of Transmission: There is little direct evidence that Hodgkin lymphoma is transmissible. However, its association with EBV indicates a need for further research. In addition, there may be a genetic predisposition to the malignancy.

Epidemiology: The American Cancer Society estimates about 9,060 new cases of Hodgkin lymphoma will be diagnosed in 2012, slightly more in men than in women. About 85 to 90% of cases are seen in adults between the ages of 15 and 40 and those older than 55 years. Only 10 to 15% of cases are seen in children and teenagers under the age of 15 (ACS, 2011).

Pathogenesis: Hodgkin lymphoma is characterized by the presence of an abnormal tumor cell (*Reed-Sternberg* cell) thought to result from malignant transformation of a B lymphocyte. Hodgkin lymphoma usually starts in a single lymph node in the upper body (cervical, supraclavicular, axillary, inguinal, or retroperitoneal) and then spreads to adjacent nodes progressing in a systematic manner from the original node to the next in the chain. Advanced Hodgkin lymphoma can spread to any organ of the body, but the spleen, bone marrow, lungs, digestive tract, and liver are the most common sites. As the disease progresses, the individual becomes highly susceptible to infection because of the associated immune system dysfunction. Increasing numbers of cancer cells block the normal function of organs, eventually causing them to shut down and resulting in death.

Extraoral Characteristics: Asymmetric painless enlargement and fixation to underlying tissues of one or more lymph nodes without reason is the first sign of this disease. The disease normally begins in the upper part of the body, specifically, the chest, neck, or under the arms. Aside from enlarged, fixed lymph nodes, other symptoms are significant weight loss, fever, drenching night sweats, pruritus (itchiness), and fatigue.

Perioral and Intraoral Characteristics: Intraoral growth of a tumor in Hodgkin lymphoma is highly unlikely; however, unilateral tonsillar enlargement may be observed in the early stages of a primary oral lesion (uncommon), and extranodal submucosal swelling with ulceration and erosion of underlying bone is possible, especially in metastatic or advanced cases (Regezi et al., 2008).

Distinguishing Characteristics: See Significant Microscopic Features

Significant Microscopic Features: Presence of the Reed-Sternberg cell in biopsy specimens from affected lymph nodes is diagnostic of this disease (Fig. 9.14).

Dental Implications: The importance of performing thorough routine head and neck and intraoral evaluations cannot be overemphasized because the dental professional may well be the first person to detect the enlarged lymph nodes associated with this disease because cervical and supraclavicular nodes are commonly involved. Any suspicious finding should prompt the dental professional to refer the individual for a definitive diagnosis.

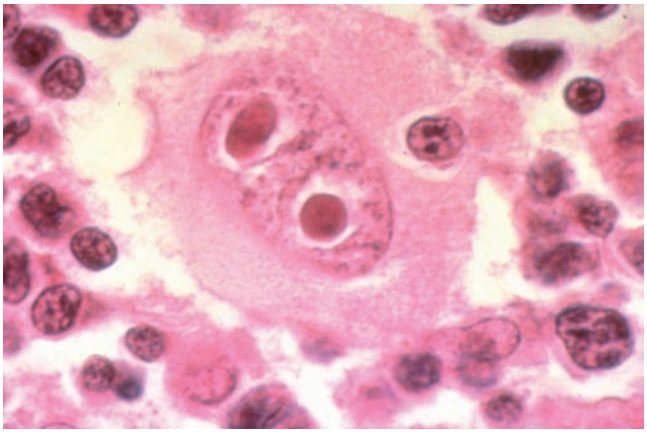

FIGURE 9.14. Reed-Sternberg cell. Mirror image nuclei are characteristic of the Reed-Sternberg cell which is diagnostic of Hodgkin lymphoma. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

Differential Diagnosis: Infectious diseases presenting with lymph node enlargement, such as mononucleosis and tuberculosis should be ruled out, as well as other forms of lymphoma, discussed in the following sections. Salivary gland tumors and disorders should also be considered.

Treatment and Prognosis: Treatment depends on the severity of the disease and microscopic appearance of the tissues. The most common treatment is a combination of chemotherapy and radiation therapy. Chemotherapy usually consists of a regimen combining multiple drugs administered over a period of time. Radiation of the involved nodes is accomplished after the completion of chemotherapy. Other treatments being used are monoclonal antibody therapy and bone marrow and stem cell transplants.

The American Cancer Society estimates that 1,190 people will die from Hodgkin lymphoma in 2012. Death rates have dropped more than 60% since 1970 because of improved therapies. The survival rates for patients are 1 year, 92%; 5 years, 85%; and 10 years, 81% (ACS, 2011).

NAME: Non-Hodgkin lymphoma

Non-Hodgkin lymphoma is a generic term used to describe a group of malignant neoplasms that arise from B lymphocytes and T lymphocytes. Approximately 85% of non-Hodgkin lymphomas are B cell neoplasms, and the remaining 15% are T cell neoplasms (ACS, 2012). Acute and chronic lymphocytic leukemia (CLL) are considered forms of lymphoma; however, these are discussed along with myelogenous leukemia in the next section.

Etiology: The etiology of most forms of non-Hodgkin lymphoma is unknown; however, changes in chromosome

structure, especially translocations involving chromosomes 18q, 11q, 14q, 12q, and 1p play an important role in the pathogenesis of lymphoma and appear to be a predisposing factor. Other risk factors associated with lymphoma include the following: (ACS, 2012; Vinjamaram et al., 2012)

- Age over 60 years
- Infection with EBV, human T-cell leukemia virus, hepatitis C virus (HCV), Kaposi sarcoma–associated herpes virus, and *Helicobacter pylori*
- Environmental exposure to ionizing radiation or chemicals (pesticides, herbicides, benzene)
- Previous chemotherapy and/or radiation therapy for other malignancies
- Immune system deficiencies such as immunosuppressive drug therapy, infection with HIV, inherited or acquired immune deficiency disorders, and celiac disease
- Chronic inflammation associated with autoimmune disorders such as Sjögren syndrome, lupus erythematosus, Hashimoto thyroiditis, and rheumatoid arthritis

Method of Transmission: Both bacterial and viral agents have been implicated in the development of non-Hodgkin lymphoma, and steps to prevent infection should be taken if possible; for example, HIV infection is preventable.

Epidemiology: The American Cancer Association estimates that 70,130 men and women will be diagnosed with non-Hodgkin lymphoma in the United States during 2012. This form of cancer is slightly more common in men than in women and 95% of cases develop in adults, half of these in patients over the age of 65. A person's risk of developing non-Hodgkin lymphoma during his or her lifetime is about 1 in 50 (ACS, 2012).

Pathogenesis: A genetic mutation not repaired by any of the mechanisms (such as DNA repair genes) in place to repair this type of genetic damage occurs during development of the lymphocyte (see Chapter 5). In addition, the cell is not destroyed by the body's defenses against neoplastic growth, as it should be. This may be due to activation of oncogenes or inactivation of tumor suppressor genes as well as others. Uncontrolled replication of the defective cell ensues, and a lymphoma develops. The organs associated with the lymphatic system are affected first, with eventual spread to any body tissue or organ.

Extraoral Characteristics: The most common clinical manifestation of the disease is superficial, nontender, fixed lymphadenopathy. The cervical, axial, and inguinal nodes are commonly the first to be affected or noticed (Fig. 9.15). Spread can be contained within contiguous nodes or the disease can spread to noncontiguous nodes and tissues. In addition to soft tissues, bones may be affected by tumors. Systemic symptoms of fever, drenching night sweats, and weight loss are not as common as in Hodgkin lymphoma, and their presence usually indicates a poor prognosis.

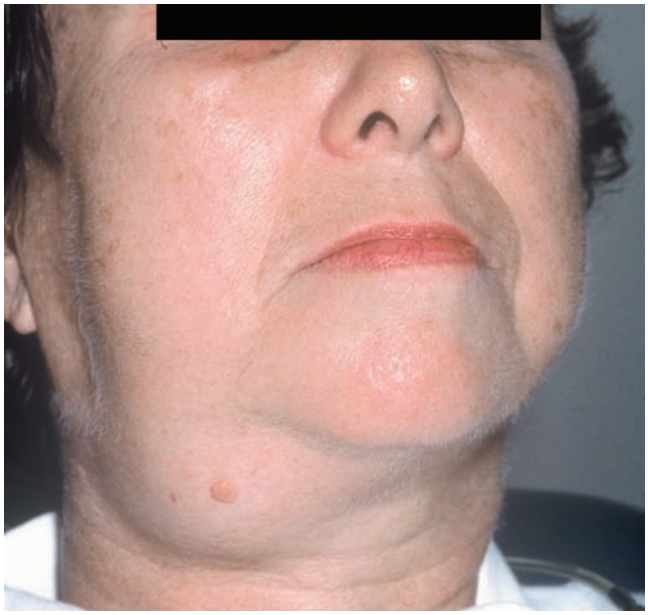

FIGURE 9.15. Lymphadenopathy. Enlarged submandibular lymph node caused by a non-Hodgkin lymphoma. (Courtesy of Dr. Michael Brennan.)

Perioral and Intraoral Characteristics: Oral manifestations of lymphoma are uncommon but when present usually appear as a soft tissue mass in the Waldeyer ring area (the tonsil is the most common oropharyngeal site), in the lymphoid tissues found at the base of the tongue, or in the major and minor salivary glands (Regezi et al., 2008). The lesions may, or may not, be ulcerated. When bone is involved, the most common intraoral site is the hard palate (Fig. 9.16). Tumors within bone, or central tumors, may present as an ill-defined radiolucency that can progress to expansion of the bone and perforation of the cortical plate, resulting in a soft tissue swelling at the site of the tumor. These tumors can cause loss of alveolar bone, tooth mobility, swelling, pain, paresthesia, and pathologic bone fractures. Figure 9.17 depicts a non-Hodgkin lymphoma of the gingiva.

Lymphomas associated with HIV infection manifest in the oral cavity more often than those associated with other causes and account for about 3% of intraoral tumors seen in individuals with AIDS (Regezi et al., 2008).

Significant Microscopic Features: The microscopic appearance of the tumor cells varies with each type of lymphoma.

Dental Implications: Medical histories should be carefully reviewed for the presence of risk factors. Head and neck examination for signs of lymphadenopathy should be performed for every patient when presenting for preventive appointments or for any new or emergency patient. Patients who present with indurated, nontender, fixed nodes should be referred immediately to a physician for further diagnosis. Intraoral swelling with or without associated radiolucencies should be definitively diagnosed.

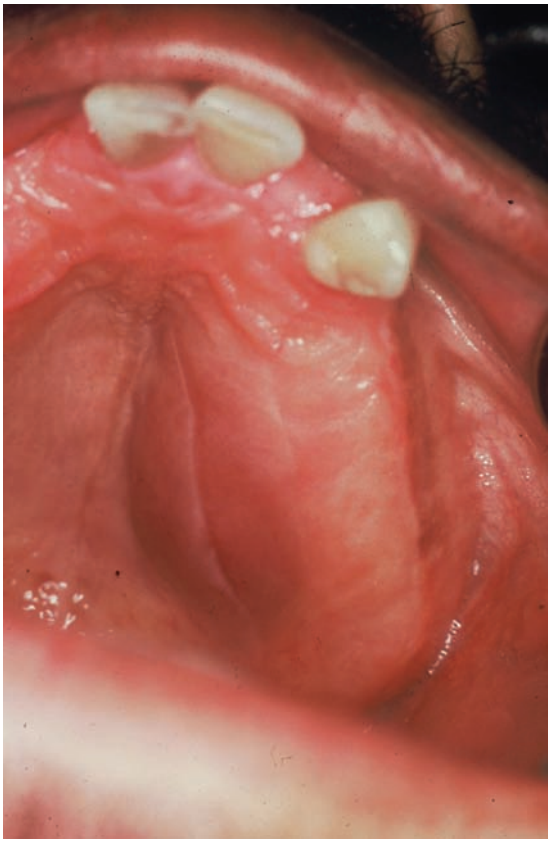

FIGURE 9.16. Oral non-Hodgkin lymphoma. Posterior palatal enlargement caused by non-Hodgkin lymphoma. (Courtesy of the United States Department of Veteran's Affairs.)

Differential Diagnosis: The differential diagnosis for non-Hodgkin lymphoma is extensive and includes such other neoplasms as:

1. Squamous cell carcinoma
2. Nasopharyngeal carcinoma
3. Thyroid carcinoma

FIGURE 9.17. Non-Hodgkin lymphoma. This exophytic mass is an example of a non-Hodgkin lymphoma found in the attached gingiva. (From Neville BW, Damm DD, White DK. Color Atlas of Clinical Oral Pathology. 2nd ed. Ontario, Canada: BC Dekker Inc., 1999. Courtesy of Brad Neville.)

Lymphadenopathy from infectious etiologies would also be included in the differential diagnosis, including:

1. Bacterial (tuberculosis)
2. Viral (mononucleosis, cytomegalovirus, HIV)
3. Parasites (toxoplasmosis)

The differential diagnosis for a central (bone) presentation of lymphoma include:

1. Metastatic neoplasms
2. Osteogenic sarcoma

These lesions need to be distinguished from one another by biopsy.

Treatment and Prognosis: Treatment depends on the type of non-Hodgkin lymphoma and the stage of the disease. Early stage lymphomas are usually very radiosensitive; therefore, radiation therapy is used aggressively in many cases. Chemotherapy is also effective and is normally given in combinations of two or more drugs taken every 2 to 4 weeks for variable lengths of time and may be combined with radiation therapy. Resistant and recurrent lymphomas may be treated with a stem cell or bone marrow transplant after high doses of chemotherapy or radiation. Additional treatments using monoclonal antibodies and targeted therapy are being used more frequently.

The prognosis also depends on the type of lymphoma and the stage of the disease when treatment is started. The American Cancer Society estimates that 18,940 men and women will die from non-Hodgkin lymphoma in 2012. The overall 5-year relative survival rate for non-Hodgkin lymphoma is about 67%, and the 10-year relative survival rate is about 55%. The relative survival rates only take into account those individuals who die from the non-Hodgkin lymphoma and not from other related causes, such as heart disease (ACS, 2012).

Burkitt Lymphoma

Burkitt lymphoma is a very aggressive form of non-Hodgkin lymphoma and is thought to be the most rapidly growing cancer known. There are three forms of the disease: (1) an endemic form found in Africa, (2) a more sporadic form seen in North America and Europe, and (3) a form that is associated with immunodeficiency. Burkitt lymphoma affects children and young adults (under the age of 35) more often than older adults, and 90% of its victims are male (ACS, 2012). In parts of Africa, Burkitt lymphoma is associated with EBV in almost all cases, while here in the United States, EBV is only associated with about 20% of cases (Kanbar & Sacher, 2011). The endemic form often manifests in the maxilla or the mandible, while the sporadic form seen in the United States presents as a mass in the abdomen, with or without bone marrow involvement (Regezi et al., 2008). Oral manifestations of the endemic form consist of rapidly expanding bone lesions that quickly deform the face (Fig. 9.18) and loosening of the affected teeth; the sporadic form manifests with oral lesions in only 10% of cases (Regezi et al., 2008). Treatment consists of intense chemotherapy with multiple drugs. In

FIGURE 9.18. Burkitt lymphoma. Burkitt lymphoma of the jaw is distorting the facial features of this African child. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

spite of the aggressive nature of this disease, the American Cancer Society estimates that 70 to 90% of persons with this form of lymphoma have survived for 5 years or longer and are usually considered cured because it is rare for this type of cancer to recur after 5 years (ACS, 2012).

Burkitt lymphoma associated with immunodeficiency disorders, specifically AIDS, is usually diagnosed at an advanced stage. Figure 9.19 depicts Burkitt lymphoma in the oral cavity of an HIV-positive male. The prognosis for these individuals is dismal because of their already compromised immune status and the individual's inability to withstand any type of aggressive therapy (Regezi et al., 2008). Death normally occurs shortly after the diagnosis.

NAME: Leukemia

The term "leukemia" describes a group of malignant neoplasms involving leukocytes. Two basic classifications denote whether the disorder involves cells derived from lymphoid stem cells (B and T lymphocytes) or cells derived from myeloid progenitor cells (granulocytes or monocytes). (Refer to Figure 9.1 for a review of the process of hematopoiesis). Further classification identifies whether the disease is acute or chronic. There are four main types of acute and chronic leukemia, listed below:

- Acute lymphocytic (or lymphoblastic) leukemia (ALL)
- Chronic lymphocytic leukemia (CLL)
- Acute myeloid (or myelogenous) leukemia (AML)
- Chronic myeloid (or myelogenous) leukemia (CML)

FIGURE 9.19. Burkitt lymphoma. This Burkitt lymphoma tumor was discovered in an HIV-positive male patient. (Courtesy of Dr. Douglas Damm.)

Etiology: Genetic mutations cause leukemia. The reason for the genetic damage is still mostly unknown. Some risk factors have been identified and include environmental exposure to radiation and certain chemicals, previous exposure to chemotherapeutic drugs, and some genetic syndromes. Table 9.4 provides more specific information regarding the etiology, epidemiology, and prognoses for the different types of leukemia.

Method of Transmission: Not applicable

Epidemiology: Refer to Table 9.4 for epidemiologic information related to the four types of leukemia.

Pathogenesis: The acute forms of leukemia usually present with symptoms within days to several weeks of the start of disease activity. The chronic forms exhibit a more insidious or gradual progression of the disease and are sometimes in advanced stages at the time of diagnosis.

There is an overgrowth of **blastic cells** (cells that fail to mature) in acute leukemia, and chronic leukemia produces stem cells that do not respond to the body's attempts to regulate their proliferation. In both instances, extremely high numbers of the abnormal (malignant) white cells are produced, increasing the viscosity (thickness) of the blood and causing an infiltration or overflow of the excess white blood cells into organs and tissues that normally contain leukocytes. In addition, the malignant cells produced do not function normally and do not fulfill their role in protecting the body against infection.

Increased production of one type of leukocyte causes an increase in the amount of marrow associated with that leukocyte, which eventually overwhelms the rest of the bone marrow. This event causes a decrease in the production of RBCs, platelets, and other nonaffected white blood cells. The symptoms of leukemia are associated with the disorders produced by the decrease in the numbers of these cells, specifically, anemia, neutropenia, and thrombocytopenia (low blood platelets).

Extraoral Characteristics: The initial symptoms of ALL and AML are similar. Patients normally exhibit symptoms associated with anemia (fatigue, pallor, etc.), infection (fever, night sweats), thrombocytopenia (epistaxis, petechiae, bruising), increased metabolic rate of the cancer cells (weight loss), bone marrow expansion (bone pain), and the infiltration of the liver, spleen, and lymph nodes by leukemic

TABLE 9.4 **Leukemia**

Type of Leukemia	Etiology	Epidemiology	Prognosis
Acute lymphocytic leukemia (ALL)	Mostly unknown 5% have Philadelphia chromosome Inherited syndromes (Trisomy 21, Klinefelter, neurofibromatosis, Bloom, etc.)	Found more often in children (66%) than in adults (33%) Peak age 2–4 years old Slightly more in males More in whites than in blacks	Cure rate for children 1 to 10 years of age is 80% Survival rate for infants under 1 year of age is 30% Adults experience a 40% long-term remission or cure rate
Chronic lymphocytic leukemia (CLL)	Mostly unknown Deletion of genetic material from chromosome 13, 11, 17 Trisomy 12 Agent Orange (herbicide used in the Vietnam War) Family history	Average age at diagnosis is 72; very rare at ages under 40 Slightly more in males	Survival time varies from 1 year to 5–10 years or more depending on the course of the disease
Acute myeloid leukemia (AML)	Mostly unknown Blood disorders (polycythemia vera, essential thrombocytopenia) Inherited syndromes (trisomy 21; neurofibromatosis, Fanconi anemia, Bloom) Prior chemotherapy for another malignancy Exposure to benzene Irradiation (accidental or therapeutic) Smoking	Average age 67 Uncommon before age 40 Slightly more in males	5-year survival rate for individuals under the age of 65 is 33%, over the age of 65 is 4% 5-year survival rate for children is 50–70%
Chronic myeloid leukemia (CML)	Mostly unknown 90% have Philadelphia chromosome High-dose radiation exposure Increasing age Slightly higher in smokers	10–15% of all leukemias Average age 65 More in men More in whites	5-year survival rate almost 100% due to treatment advances Survival rate after 5 years has not been determined

cells, causing enlargement of these organs. Leukemic infiltration of the skin can cause pruritus. Infiltration of the central nervous system is more common in ALL than in AML and can cause headache, nerve dysfunction, nausea, vomiting, and sometimes seizures. Hyperviscosity of the blood caused by leukocytosis (leukocyte levels of 100,000 cells/mm^3) can effectively plug up the microvasculature, causing infarcts and vessel rupture in the lungs, brain, and other organs.

Chronic leukemia may be present for years without being noticed and may only be discovered while performing routine blood work. Symptoms of CLL are usually not apparent at diagnosis but appear slowly as the bone marrow is gradually overtaken by the production of lymphocytes. Symptoms include those associated with anemia, neutropenia, and thrombocytopenia. Repeated infections, increasing fatigue, enlargement of the lymph nodes, increased bleeding tendencies, and bone pain signal progression of the disease. The course of CML differs from that of CLL because it progresses through three distinct phases:

1. The first, or chronic, phase is characterized by leukocytosis that is well controlled by medication and can last for 2 to 10 years or more. During this phase, the symptoms associated with anemia, neutropenia, and thrombocytopenia are minor or not noticed by the patient.
2. The second, or accelerated, phase is associated with loss of medical control of the disease and is characterized by increasing numbers of leukemic cells and the appearance of more severe symptoms associated with anemia, neutropenia, and thrombocytopenia. Weight loss can be expected due to the high nutritional needs of the proliferating malignant cells.
3. The last phase is called the acute phase, or blast crisis, and is preceded by bone pain and fever. More severe symptoms are seen in this stage, and the leukemic cells tend to infiltrate the skin, bones, lymph nodes, and central nervous system. Infarcts and hemorrhage due to leukocytosis are more common in this phase. Survival after the initiation of a blast crisis is counted in months.

Perioral and Intraoral Characteristics: Oral findings in all types of leukemia include increased gingival or periodontal infections, increased gingival bleeding, unexplained petechiae or purpura in the oral soft tissues, and gingival enlargement due to leukemic infiltrate (Fig. 9.20). Gingival enlargement is seen most often in CML. Many patients seek dental care prior to medical care because of the rapid decline in oral health and appearance of the tissues.

FIGURE 9.20. Gingival enlargement. Leukemic infiltrate associated with acute myeloid leukemia (AML) has caused the gingival enlargement seen in this picture. Superficial inflammation is associated with oral candidiasis. (Courtesy of the Council on Dental Therapeutics, the American Dental Assn. and the Public Health Image Library. Available at: http://phil.cdc.gov/phil/home.asp File 6049).

Distinguishing Characteristics: The *Philadelphia chromosome* (created when translocation of genetic material occurs between chromosomes 9 and 22) is present in approximately 90% of CML and about 5% of ALL cases. The presence of this chromosomal aberration is the basis for the targeted drug therapies that are driving 5-year survival rates to almost 100% for CML (ACS, 2011).

Significant Microscopic Features: Microscopic features vary according to the type of leukemia.

Dental Implications: The clinician must investigate any case of gingival or periodontal inflammation or infection that does not respond to normal interventions, especially if other systemic manifestations, such as fever, weight loss, or night sweats are present. Patients should be referred to their physician for further evaluation. Elective dental care would not be appropriate during periods when bleeding is excessive or white cell counts are low. Consultation with the oncologist to determine adequate levels of white blood cells and the International Normalized Ratio (INR) should precede any dental or dental hygiene care. Stress good oral hygiene to help prevent exacerbating already compromised oral health and potential systemic infection.

Differential Diagnosis: The gingival enlargement associated with leukemia could be caused by hormonal influences in puberty or pregnancy or associated with drugs such as calcium channel blockers (antihypertensive), phenytoin (antiseizure), and cyclosporine (immunosuppressive).

Treatment and Prognosis: The traditional treatment for acute leukemia of either type is aggressive chemotherapy. This may be augmented by treatment with *monoclonal antibodies*. Monoclonal antibodies are produced by engineered cells made in the laboratory by fusing tumor cells that grow continuously with mammalian cells that can produce antibodies. The resulting engineered cells replicate continuously and produce large amounts of antibody against the tumor cells. The antibody produced can be engineered to target just about any cell or portion thereof, such as a particular protein or enzyme. Several monoclonal antibodies are being used to treat the different forms of leukemia. Other types of drugs developed to target and inhibit proliferation of cells containing the Philadelphia chromosome comprise targeted therapy and include imatinib (Gleevec) and dasatinib (Sprycel), among others. These oral drugs are being used successfully as the primary treatment for most cases of CML and some cases of ALL. Both monoclonal antibodies and targeted therapy drugs affect only abnormal cells, which results in fewer side effects and a better quality of life.

Bone marrow and peripheral blood stem cell transplants are an option for treating ALL, AML, and CML. Both of these procedures require the individual's bone marrow cells to be destroyed by high doses of chemotherapy, radiation, or both. After the cells are destroyed, the transplant cells are infused into the bloodstream, where they will go to the bone marrow and begin to produce new normal blood cells. Neither bone marrow transplants nor stem cell transplantation is indicated for the treatment of CLL.

Supportive treatment includes using antibiotics, antifungals, and antivirals to control or prevent infections. Low platelet counts might require a transfusion of platelets to control bleeding. Anemia is often treated with drugs that stimulate the production of red cells or red cell transfusions. Neutropenia caused by the disease and the treatments can be treated with drugs that increase the production of these cells. Refer to Table 9.4 for the prognoses of the different types of leukemia.

NAME: Multiple myeloma

Etiology: Multiple myeloma, a B-cell cancer, results in the overproduction of malignant plasma cells (the cells responsible for producing immunoglobulins) and is associated with acquired genetic abnormalities involve the creation of oncogenes and mutation of the tumor suppressor gene p53. The genetic abnormalities have been linked to environmental radiation, such as nuclear accidents, and with the accumulation of genetic errors occurring within our cells as we age. Obesity and a family history of the disease are considered risk factors as well as working in certain petroleum-related industries (ACS, 2012). The deletion of pieces of chromosome 13 has been associated with a very aggressive form of the disease (ACS, 2012).

Method of Transmission: There may be a slight genetic tendency because there is a higher rate of disease within first-degree relatives (mother, father, sisters, and brothers) and because of the significantly higher rate in blacks.

Epidemiology: The American Cancer Society estimates that 21,700 Americans (9,250 men and 7,320 women) will be diagnosed with this disease in 2012. Blacks develop this

disease two times more often than whites, and men are affected more often than women. Most people with this disease are over 65 years of age (ACS, 2012).

Pathogenesis: The manifestations of this disease are caused by (1) excessive production of an abnormal immunoglobin (monoclonal paraprotein) called M-protein, which causes a decreased production of all other immunoglobulins resulting in immunosuppression; (2) increased activation of osteoclasts, which results in bone resorption; and (3) the production of an abnormal protein called *Bence Jones protein* that is excreted in urine. Because protein is not normally eliminated through the kidneys, the Bence Jones protein accumulates in the kidney tubules, eventually causing renal failure (Seiter et al., 2012; ACS, 2012).

Extraoral Characteristics: The most common presenting feature of multiple myeloma is related to infiltration of the bone by the plasma cells and the activation of osteoclasts, resulting in bone resorption, pathological fractures, and bone pain. The vertebrae, ribs, skull, pelvis, and femur are most frequently affected. Localized and generalized infections, especially bacterial infections, are caused by the lack of normal immunoglobulins, excessive M-protein, and suppression of leukocyte production in affected bone marrow. Renal failure results from high calcium levels in the blood (hypercalcemia) and damage done by the Bence Jones protein. The most common causes of death are severe infection or renal failure. There are two other forms of the disease: (1) solitary plasmacytoma and (2) extramedullary plasmacytoma.

The solitary plasmacytoma is seen as a single area of bone destruction, usually in the vertebrae, ribs, or pelvis. It is rarely seen in the oral cavity. Some 30 to 75% of these cases progress to multiple myeloma (Regezi et al., 2008).

Plasma cell tumors that are found in soft tissues are called extramedullary plasmacytomas. Most of these tumors (80%) are found in the upper respiratory tract and the oral environment (Regezi et al., 2008). These tumors present as exophytic red masses that usually do not ulcerate. Progression to multiple myeloma is rare in these individuals.

Perioral and Intraoral Characteristics: Bone lesions in the skull are common and manifest as multiple, well-defined, radiolucent areas that appear "punched out" from the surrounding bone (Fig. 9.21). Jaw lesions are seen more in the mandible than in the maxilla, and they are found more often in the posterior areas (Regezi et al., 2008). Some of the abnormal immunoglobulins created by this disease combine to form what is called amyloid, an abnormal protein deposited in tissues throughout the body such as the heart, lungs, or kidneys, where it causes tissue enlargement and interferes with normal functioning. Amyloid accumulation is quite often seen in the tongue as macroglossia (Fig. 9.22). The immunosuppressive nature of this disease increases the risk that these individuals will have some form of periodontal infection.

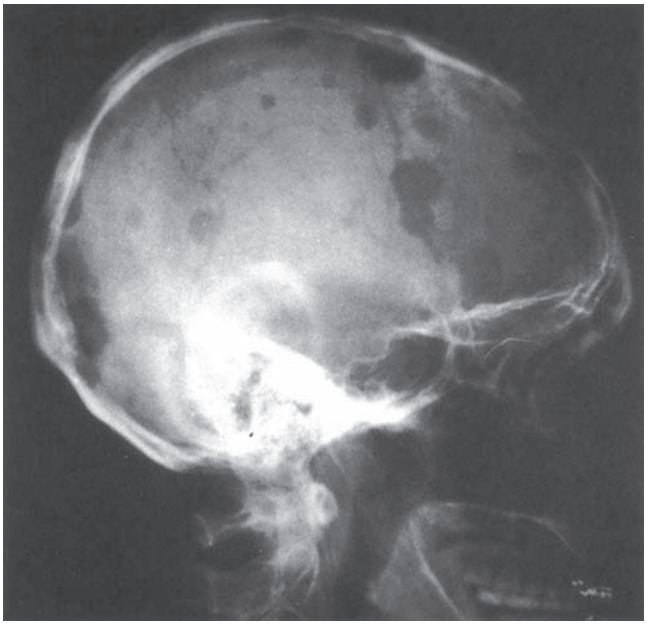

FIGURE 9.21. Multiple myeloma. A radiograph of the skull shows the "punched-out" radiolucent lesions characteristic of multiple myeloma. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

Distinguishing Characteristics: The "punched-out" radiographic lesions are characteristic of this disease.

Significant Microscopic Features: Bone marrow samples containing over 30% plasma cells are indicative of this disease.

Dental Implications: Dental hygiene/dental care should focus on controlling infections associated with a compromised immune system. Tests to determine white cell levels should be ordered or results obtained from the patient's physician prior to performing dental or dental hygiene

FIGURE 9.22. Macroglossia. This is an example of macroglossia caused by the deposition of amyloid proteins within the tongue. Note the scalloping from pressure the tongue is exerting on the lingual surfaces of the teeth. (From Stedman's medical dictionary for the health professions and nursing, 5th ed. Baltimore: Lippincott Williams & Wilkins, 2005.)

procedures with a significant risk of bacteremia. Clotting time or the INR should also be determined if indicated, for example, patients who suffer from thrombocytopenia associated with a decrease in platelets or some patients who are receiving anticoagulant medications to counteract an increased risk of thrombus formation associated with some drugs used to treat multiple myeloma such as thalidomide. Many patients with multiple myeloma who are treated with bisphosphonates must be monitored closely for osteonecrosis of the jaw. It is the dental professional's responsibility to educate the patient about the necessity of reporting unusual sores or painful areas in the mouth and the importance of maintaining immaculate oral hygiene.

Differential Diagnosis: The presence of only intraoral manifestations necessitates ruling out any disorder causing well-defined radiolucent bone lesions. These include:

1. Traumatic bone cyst, Chapter 20
2. Langerhans cell disease, Chapter 20
3. Metastatic cancer, Chapter 5

Macroglossia could be the result of the following:

1. Acromegaly, Chapter 7
2. Trisomy 21, Chapter 6
3. Lymphangioma, Chapter 17
4. Vascular malformation, Chapter 13
5. Neurofibroma, Chapter 17
6. Amyloid accumulation as a result of another chronic illness

Exophytic red soft tissue masses found in the oral cavity include:

1. Pyogenic granuloma, Chapter 13
2. Peripheral giant cell granuloma, Chapter 13
3. Kaposi sarcoma, Chapters 13 and 22
4. Squamous cell carcinoma, Chapters 5 and 12

Treatment and Prognosis: There is no known cure for multiple myeloma. In general, multiple myeloma is treated with chemotherapy. Combinations of different drugs have been shown to have the best results. Multiple myeloma is very sensitive to radiation therapy, which is used for solitary or painful bone lesions, to strengthen weak areas of bone and for bone lesions not responding to chemotherapy. Drugs used to treat osteoporosis like bisphosphonates that interfere with osteoclast activity help to prevent further damage and permit osteoblasts to strengthen weakened areas. Stem cell transplantation may be a treatment option for some patients. Individuals with this disorder may go into remission for many years or may not be able to control the disease from the outset. The relative 5-year survival rate is 40% (ACS, 2012).

Hemostasis

Hemostasis is the process by which the body prevents blood loss from injury. Platelets and circulating coagulation factors are the major participants in the maintenance of hemostasis.

BOX 9.2 **Coagulation Factors**

Factor I	Fibrinogen
Factor II	Prothrombin
Factor III	Tissue factor
Factor IV	Calcium
Factor V	Proaccelerin
Factor VII	Proconvertin
Factor VIII	Antihemophilic factor
Factor IX	Plasma thromboplastin
Factor X	Stuart-Prower factor
Factor XI	Plasma thromboplastin antecedent
Factor XII	Hageman factor
Factor XIII	Fibrin-stabilizing factor

Platelets are created from megakaryocytes, which are derived from the same pluripotential stem cells that create red and white blood cells. The nuclear material in the megakaryocyte undergoes division but the cytoplasm does not. The cell expands to hold the extra DNA, but is unsuccessful and breaks up into small pieces called platelets (see Fig. 9.1).

There are 12 numbered coagulation factors found in blood plasma (see Box 9.2). The numbers indicate the order in which factors were discovered, not the order in which they work and the number 6 was omitted. Vitamin K is necessary for the production of most of the factors and almost all of the factors are produced in the liver. Calcium (factor IV) is necessary for all but the first two reactions that take place in the cascade. Cascade systems, such as the coagulation cascade, consist of a series of inactive enzymes. Once the first enzyme or, in this case, coagulation factor in the series is activated, it initiates the next in a series of reactions in which the product of the last reaction is the initiator of the next reaction. The coagulation cascade is illustrated in Figure 9.23. The coagulation cascade ends when thrombin converts fibrinogen into fibrin, which forms the substance of a blood clot. It is not important to remember the specific names of the factors, but it is important to realize a defect at any point in the cascade or in the substances initiating the cascade can result in malfunction of the clotting system and uncontrolled blood loss.

Specific events must occur in sequence to achieve hemostasis in the face of vascular injury. The initiating event causes damage to the body and bleeding. The involved vessels immediately constrict to limit the loss of blood. The damaged endothelial cells release von Willebrand factor (vWF), which literally grabs the circulating platelets causing them to adhere to the injured vessel wall. Other substances released by the platelets cause the adherence of more platelets, creating a "platelet plug." While the platelet plug is forming, the coagulation cascade is being activated

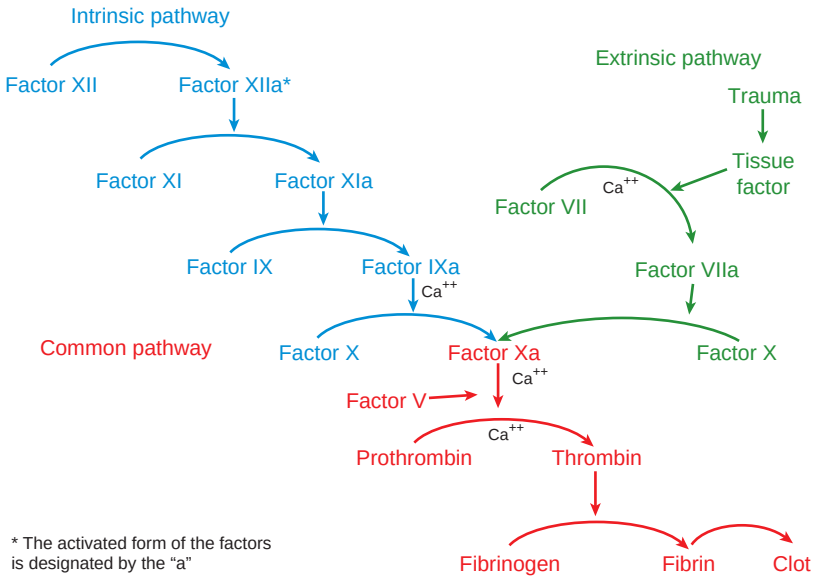

FIGURE 9.23. Coagulation cascade. The coagulation cascade is initiated when factor XII (Hageman factor) contacts an injured endothelial surface (intrinsic pathway) or when tissue factor (released by damaged endothelial cells) comes in contact with factor VII in the plasma (extrinsic pathway). Intrinsic and extrinsic pathways converge at the activation of factor X (Xa) and follow a common pathway that results in clot formation.

and fibrin strands are being created to reinforce the platelet plug, making it stable and insoluble (Fig. 9.24).

Hemostasis can be compromised by an insufficient number of platelets, dysfunction of the platelets, or defective coagulation factors. The end result of compromised hemostasis is either hypercoagulation (overproduction of clots) or bleeding disorders. Hypercoagulation is discussed briefly earlier in this chapter under "Polycythemia" and in Chapter 8 regarding thrombus formation associated with atherosclerosis. Table 9.5 lists common blood tests used to evaluate hemostasis.

FIGURE 9.24. Fibrin clot. Scanning electron micrograph of a blood clot (3 × 600). The filaments forming a meshwork between the RBCs are fibrin fibers formed as an end product of the coagulation cascade. (From Porth CM. Essentials of pathophysiology: concepts of altered health states. Philadelphia: Lippincott Williams & Wilkins, 2006.)

NAME: Bleeding disorders

Etiology: The etiology and method of transmission of select bleeding disorders are listed in Table 9.6.

Method of Transmission: See Table 9.6.

Epidemiology: The National Hemophilia Foundation estimates hemophilia A affects 1 in every 5,000 male births and hemophilia B affects 1 of every 25,000 male births. von Willebrand disease is the most common inherited platelet disorder, affecting 1 to 2% of the United States population, both male and female (NHF, 2006).

Pathogenesis: Hemophilia A (factor VIII) and B (factor IX) are associated with a deficiency or defect in their respective factors, which results in defective or inadequate clot formation. von Willebrand disease is associated with defective or inadequate levels of vWF causing defective or inadequate platelet adhesion to sites of injury. In addition, since vWF carries factor VIII, there may be a concomitant deficiency of this factor, which would add defective clot formation to the platelet disorder. Acquired bleeding disorders (bleeding disorders caused by factors other than genetic factors) are often associated with liver disease because coagulation factors are manufactured in the liver, inadequate absorption of dietary vitamin K (malabsorption syndromes such as irritable bowel syndrome, Crohn disease, and celiac sprue) and dietary deficiency of vitamin K (alcoholism and malnutrition). Normally, vitamin K is produced by the bacteria living in our intestines making it almost impossible to have

TABLE 9.5 **Blood Tests that Evaluate Hemostasis**

Test	Normal Values	Etiology of Abnormal Findings
Platelet count Determines if there is an adequate number of platelets	150,000–450,000/mm^3[a]	Increased—polycythemia, CML, sickle cell anemia, and other hemolytic anemias Decreased—ALL, AML, liver disease, thrombocytopenia, pernicious and aplastic anemia
Bleeding time Evaluates the function of platelets	3–10 minutes[a]	Increased (prolonged)—platelet disorders, thrombocytopenia, leukemia, von Willebrand disease, antiplatelet drug therapy (aspirin)
Partial thromboplastin time, activated (aPTT) Evaluates the time it takes to form a fibrin clot when calcium and tissue factor are added to the plasma (intrinsic pathway)	21–35 seconds[a]	Increased (prolonged)—hemophilia, von Willebrand disease, anticoagulant therapy
Prothrombin time (PT) Evaluates the time it takes to form a fibrin clot when a platelet factor and a surface activating factor are added to the plasma (extrinsic pathway)	11–14 seconds[a]	Increased (prolonged)—anticoagulant therapy, prothrombin deficiency, vitamin K deficiency, liver disease, polycythemia, antiplatelet drugs
Clotting Time Measures the time it takes for a clot to form in a glass tube	5–15 minutes	Increased (prolonged)—anticoagulant therapy, vitamin K deficiency, hemophilia, liver disease
International Normalized Ratio (INR)	2–3	Expresses prothrombin time as a ratio to thromboplastin activity

[a]Normal values may differ among individual laboratories.

a deficiency. However, anything that disrupts or destroys the normal intestinal flora (bacteria) such as long-term use of broad-spectrum antibiotics might also cause a deficiency of vitamin K and produce an acquired bleeding disorder.

It might be thought bleeding disorders would only be a problem with traumatic injury; however, the human body is a very complex machine and there are many opportunities for minor, even microscopic, injuries to occur on a daily basis. Normally, these injuries are inconsequential but individuals with a bleeding disorder need to be concerned about them since they cannot avoid them and have no way to know they have occurred until it is too late. The disorders may cause mild, moderate, or severe disease, and the major clinical manifestations are all associated with excessive bleeding.

TABLE 9.6 **Bleeding Disorders**

Name	Etiology	Method of Transmission
von Willebrand disease	Inadequate or defective von Willebrand factor (vWF)	Autosomal dominant or recessive; dominant is less severe Acquired; damage due to aortic valve stenosis
Hemophilia A (classic hemophilia)	Factor VIII deficiency	X-linked recessive disorder
Hemophilia B (Christmas disease)	Factor IX or Christmas factor deficiency	X-linked recessive disorder
Acquired deficiency of coagulation factors	Liver disease Vitamin K deficiency	Not applicable

Extraoral Characteristics: All of the disorders exhibit a full range of severity of bleeding, from unnoticed and undiagnosed, to severe and spontaneous hemorrhages. The severity depends on the amount and activity of the associated coagulation factor or platelet defect. Excessive bleeding in response to minor trauma is consistent throughout all of the disorders. Bleeding into the joint spaces **(hemarthrosis)** is a sign of moderate or severe dysfunction. The bleeding causes joint deformity and severe pain and usually occurs in the weight-bearing joints (Fig. 9.25). Bleeding into the muscles of the arms and legs and into the gastrointestinal tract is also common. Ninety percent of patients will have bleeding within the urinary tract, leading to blood in the urine, or **hematuria**. Women with bleeding disorders usually have heavy menstrual flow and may have excessive loss of blood during the birth of a child. Childbirth can be life threatening to a woman with a severe bleeding disorder. The most serious form of bleeding is intracranial hemorrhage, or bleeding into the brain. Patients with a severe bleeding disorder have a 10% lifetime chance of intracranial hemorrhage (Zaiden et al., 2011). The symptoms and sequela of the hemorrhages are mostly identical to those

FIGURE 9.25. Hemarthrosis. This condition results from repeated bleeds into the joint spaces. (From Lee G, Foerster J, Lukens J, et al. Wintrobe's clinical hematology, 10th Edition. Philadelphia: Lippincott -Williams & Wilkins, 1998.)

seen with stroke (Chapter 8). Most of these patients exhibit easy bruising and those with von Willebrand disease may exhibit petechiae on the skin and mucous membranes.

Perioral and Intraoral Characteristics: Many of the less severe disorders will be asymptomatic or will present with minor gingival bleeding and petechiae on the oral mucous membranes or around the lips. Spontaneous gingival hemorrhage or bleeding after minor trauma occurs frequently in those with severe bleeding disorders, and the tendency for hemorrhage is exacerbated by the presence of gingival or periodontal infections. Significant bleeding will occur after periodontal surgery or nonsurgical therapy, tooth extraction, or oral trauma of any type. In fact, excessive bleeding after dental extractions may be the first indication of a minor bleeding disorder.

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: The clinician should be curious when there is unexplained bleeding, especially in the absence of trauma or periodontal infection. Referral to a physician should be made based on the presenting oral conditions, the concomitant presence of systemic symptoms such as lymphadenopathy, fever, or weight loss, and the previous medical/dental history. Many patients are afraid to seek dental care, and regrettably, many dental professionals are reluctant to provide treatment for them. Treatment can be accomplished safely in a normal dental environment for all but the most severely affected patients. Consult with the hematologist prior to treatment to discuss the type and severity of the factor deficiency, need for prophylactic antibiotic premedication because of a joint replacement or central venous line, nature of the planned dental procedure, and recommendations for hemostatic control before, during, and after the procedure. The hematologist will request appropriate laboratory tests to determine the patient's current factor levels and clotting capabilities. Some surgical procedures will require daily factor infusion starting several days prior to the procedure. Others will only require infusion on the day of the procedure. Local anesthesia is not contraindicated in persons with hemophilia, but the factor level should be raised to at least 50% of normal before giving a mandibular block injection, because the mandibular block can cause major bleeding in the area of the neck. In most cases, buccal infiltration and intrapapillary and intraligamentary injections require only local hemostatic measures and are preferable to the mandibular block (Brewer & Correa, 2006). Oral rinses with fibrin and/or tranexamic acid (a preparation that enhances clot formation) and oral administration of epsilon aminocaproic acid (a substance that prevents destruction of a clot) can help maintain hemostasis until any sutures placed during treatment have been removed and healing has occurred. Gel foam, an absorbable gelatin sponge that provides a framework for clot formation, can be soaked in a thrombin solution and then used in an extraction site to help to control bleeding. Dental care that stresses prevention and anticipates problems is essential for the maintenance of oral health in those with hemophilia (Brewer & Correa, 2006). The infusion treatments are extremely expensive; therefore, measures should be taken to decrease the frequency of performing them. Everyday occurrences, such as the exfoliation of primary teeth, while bothersome to the normal child, can cause a severe loss of blood in the child with hemophilia. Spontaneous bleeding is often associated with severe periodontal infections in normal individuals so even slight gingival infections can cause severe bleeding for someone with hemophilia. Chlorhexidine gluconate may help minimize gingival inflammation prior to periodontal therapy. Education should stress the importance of maintaining healthy tissues, which could possibly eliminate the need for factor replacement therapy before routine dental care (Brewer & Correa, 2006).

Differential Diagnosis: Any condition that causes decreased clotting or excessive bleeding should be ruled out. Some of these are:

1. Leukemia, Chapter 9
2. Thrombocytopenia, Chapter 9
3. Agranulocytosis or cyclic neutropenia, Chapter 9
4. Antithrombotic therapy, Chapter 8
5. Hereditary hemorrhage telangiectasia, Chapter 13
6. Vitamin C deficiency

Treatment and Prognosis: All of the bleeding disorders are treated with replacement of the missing or defective factor. Hemophilia A requires infusion with concentrated factor VIII, and hemophilia B requires infusion with factor IX. von Willebrand disease requires replacement of vWF. Because factor VIII depends on the presence of vWF to function correctly, both substances are usually given at the

same time. Factor infusion is normally done prophylactically to maintain an adequate level of factor in the blood to prevent bleeding. It can also be done on demand to stop bleeding.

Desmopressin acetate, a hormone that mimics the action of vasopressin to release factor VIII from endothelial cells, is used in some cases of von Willebrand disease and mild hemophilia. It comes in an injectable form or nasal spray; both are used to stop current bleeding or as a prophylactic and are administered no more than once daily. Medications containing aspirin or any of the nonsteroidal antiinflammatory drugs should not be taken. Even some over-the-counter herbal preparations are dangerous for someone with a bleeding disorder, for example, garlic, ginger, ginkgo, and ginseng, among others.

Mild and moderate forms of hemophilia and von Willebrand disease have an excellent prognosis for a normal life expectancy. Severely affected individuals have a life expectancy of 50 to 60 years, compared with 11 years in the 1960s. Prior to mid-1980, the supply of blood, factors, and other products derived from blood were not safe from viral contamination. By 1983, over 50% of those with hemophilia were HIV positive and over 98% of those treated with plasma-derived clotting factors prior to 1985 became infected with hepatitis C. Many of these individuals with both diseases are still living but many more have already died. Advances made since then ensure the blood supply is free of contaminants, and no cases of HIV or HCV infection due to blood or blood products have been reported since 1986 and 1997, respectively (NHF, 2006). The supply of factor and blood products is safer than ever, and new developments in treatment and prevention are occurring regularly.

NAME: Thrombocytopenia

Etiology: Thrombocytopenia occurs when the platelet count drops below 150,000/mm^3 of blood resulting in an increased risk of bleeding; levels below 10,000/mm^3 are associated with spontaneous blood loss or hemorrhage (Rubin et al., 2012). Thrombocytopenia results from decreased production, ineffective production, or increased destruction of the platelets. Aplastic anemia, chemotherapy, radiation therapy, and some types of drugs all have the potential to produce this disorder. Some of the more common drugs in addition to cytotoxic drugs used in chemotherapy include thiazide diuretics, ibuprofen, tamoxifen, phenytoin, and ranitidine. Individuals who abuse alcohol are at risk for this disorder because alcohol has the potential to suppress platelet production. Several forms of rare inherited disorders also suppress the production of platelets.

Immune (idiopathic) thrombocytopenia purpura (ITP), discussed below, occurs when platelets are destroyed by antiplatelet antibodies created by the immune system. Most often, ITP is associated with leukemia, HIV infection, and collagen disorders such as systemic lupus but it may occur without any known risk factors. Children may present with temporary ITP after a viral illness.

Method of Transmission: Not applicable

Epidemiology: ITP is seen in about 7 of 100,000 adults and 5 of 100,000 children. More adult females than males are affected, but both sexes are equally affected in children. The peak age at diagnosis is 2 to 4 years in children and 20 to 50 years in adults (Silverman, 2011). No statistics are available for thrombocytopenia secondary to another disorder.

Pathogenesis: Regardless of cause, there is a severe decrease in the numbers of circulating platelets. Since platelets are essential for proper hemostasis, most of the clinical manifestations are related to impaired clot formation.

Extraoral Characteristics: Petechial hemorrhages in the skin of the lower extremities, easy bruising, purpura, epistaxis, heavy menstrual flow, gastrointestinal bleeding, and retinal hemorrhages are characteristic of platelet deficiency.

Perioral and Intraoral Characteristics: Gingival bleeding is one of the most common presenting features of thrombocytopenia. Petechiae and hemorrhagic bullae within the oral mucosa and lips are also common (Fig. 9.26).

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: The bone marrow will show increased numbers of megakaryocytes created to increase the number of platelets.

Dental Implications: Any unexplained excessive oral bleeding should prompt the clinician to refer the patient to a physician for further evaluation. If excessive bleeding occurs during dental treatment, the same type of local hemostatic measures used in other bleeding disorders should be used. In addition, platelet levels should be determined by blood tests prior to dental/dental hygiene therapy.

Differential Diagnosis: Any condition that can cause decreased clotting or excessive bleeding should be ruled out. Some of these include:

1. Leukemia, Chapter 9
2. Hemophilia, Chapter 9
3. von Willebrand disease, Chapter 9
4. Agranulocytosis or cyclic neutropenia, Chapter 9
5. Anticoagulant therapy, Chapter 8
6. Hereditary hemorrhage telangiectasia, Chapter 13
7. Vitamin C deficiency

Treatment and Prognosis: The treatment for these disorders depends on the cause or suspected cause. Thrombocytopenia associated with the use of drugs can usually be reversed by eliminating the drug. Thrombocytopenia caused by cancer treatments usually resolves with the termination of treatment. ITP is treated with transfusions of platelets, steroids to inhibit the production of antibodies, and intravenous immunoglobulin infusions.

Children usually recover within 6 to 8 weeks, with 89% eventually achieving full recovery. Only about 64% of adults

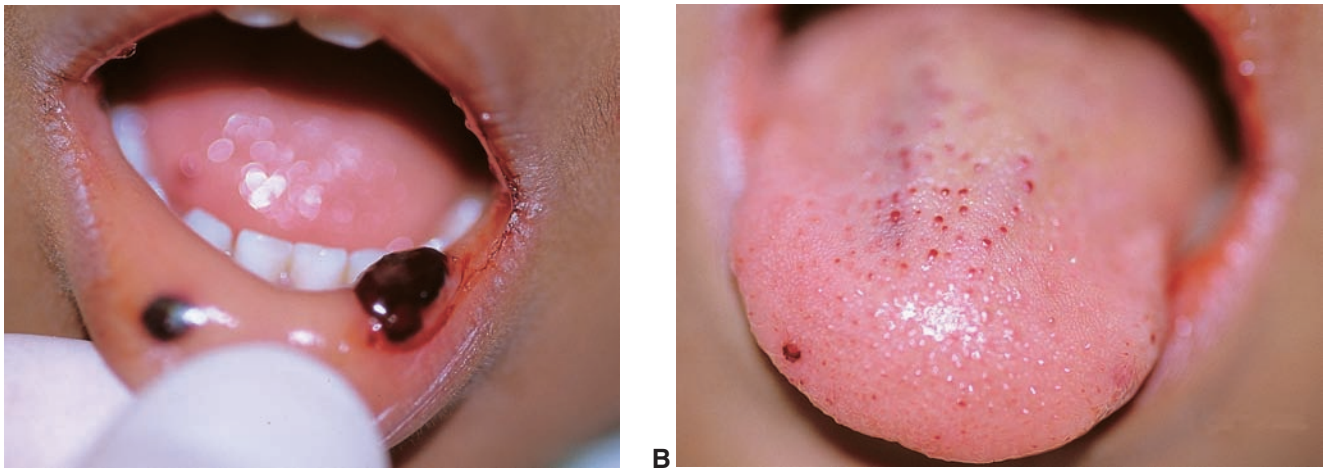

FIGURE 9.26. Immune thrombocytopenic purpura. This child presents with areas of hemorrhage in the tissues of the lip **(A)** and petechiae on the tongue **(B)** that are characteristic of this disorder. (From Fleisher GR, Ludwig W, Baskin MN. Atlas of pediatric emergency medicine. Philadelphia: Lippincott Williams & Wilkins, 2004.)

recover fully; 30% have chronic dysfunction. Mortality rates for children and adults are 2 and 5%, respectively.

Nonthrombocytopenic Purpura

Nonthrombocytopenic purpura is associated with vascular disorders as opposed to platelet disorders and results in mild bleeding disorders characterized by easy bruising and spontaneous formation of cutaneous or mucosal petechiae or purpura. This occurs due to structurally weak vessels or because of vascular damage resulting from chronic inflammation or immune system disorders, and others including vitamin C deficiency, hemorrhagic telangiectasia, Cushing disease, and older age (senile purpura).

SUMMARY

- Lymph tissue, bone marrow, and the circulating blood form the hematopoietic system. Hematopoiesis, the process of red and white blood cell production, occurs in the bone marrow.
- The pluripotential stem cells that reside in the marrow differentiate into the three types of blood cells: red, white, and platelets.
- The normal life span of an erythrocyte (red blood cell [RBC]) is about 120 days. The kidney regulates the process of erythropoiesis by secreting erythropoietin when a low blood oxygen level is sensed. Old or damaged erythrocytes are removed from the circulation by the spleen.
- Anemia manifests as a decreased level of oxygen in the blood and can be caused by a decrease in the number of cells, amount of hemoglobin, or a defect in the structure or function of hemoglobin.
- The symptoms associated with anemia include tachycardia, palpitations, dyspnea, dizziness, weakness, and fatigue. Glossitis, a common oral manifestation, occurs with many forms of anemia.
- Hypochromic or iron deficiency anemia can be due to inadequate dietary intake of iron or chronic blood loss as seen in gastrointestinal ulcers or heavy menstruation. Physical manifestations range from mild to severe, depending on the severity of the deficiency. Oral manifestations include pale mucous membranes, glossitis, oral ulcers, and angular cheilitis.
- Plummer-Vinson syndrome, a form of severe long-standing iron deficiency anemia, is associated with increased risk of developing esophageal and oropharyngeal cancers.
- Thalassemia is a group of genetic disorders that cause the formation of a defective hemoglobin molecule. The different forms of thalassemia make up the most common inherited disorders in the world.
- Megaloblastic anemia occurs when defective RNA or DNA synthesis results in the production of abnormally large red cells. Vitamin B_{12} and folic acid deficiencies are the most common cause of megaloblastic anemia.
- Pernicious anemia is an autoimmune condition that inhibits the production of intrinsic factor (IF), necessary for the transportation of vitamin B_{12} across the gastrointestinal mucous membranes. Pernicious anemia presents with the general and oral symptoms of anemia plus neurologic problems such as paraesthesia, loss of proprioception, and ataxia.
- Folic acid deficiency presents with all of the symptoms of pernicious anemia except the neurologic symptoms. Folic acid deficiency has been linked to an increased risk for NTDs, such as spina bifida, and may be linked to oral clefting.
- Sickle cell anemia, a form of hemolytic anemia, is an autosomal recessive genetic disorder that results in the production of defective hemoglobin molecules that become misshapen (sickled) when exposed to specific conditions, such as hypoxia and dehydration. Sickled cells tend to get trapped in the microvasculature and cause tissue infarcts among other problems.

- Anemia can be a secondary complication of many chronic disorders.
- Aplastic anemia occurs when disruption of the bone marrow limits or stops production of all three types of blood cells.
- Polycythemia refers to an increase in blood cells in relationship to blood plasma. Relative polycythemia occurs when there is a decrease in plasma fluid related to dehydration. Primary polycythemia occurs when there is an increase in all types of cells, usually resulting from a neoplastic disease. In secondary polycythemia, only RBCs increase.
- Neutropenia (agranulocytosis) refers to an abnormal decrease in the numbers of neutrophils. The most common cause of neutropenia is an adverse reaction to a drug. Severe periodontal disease resulting in tooth loss is associated with the chronic forms of neutropenia (cyclic neutropenia).
- Hodgkin lymphoma often presents in the head and neck area as cervical lymphadenopathy. The Reed-Sternberg cell differentiates this lymphoma from other types of lymphoma.
- Non-Hodgkin lymphoma refers to a diverse group of neoplasms arising from T and B lymphocytes. Patients who are HIV positive have a higher risk of developing non-Hodgkin lymphoma than the general population. Intraoral non-Hodgkin lymphoma may present as a soft tissue swelling in the area of Waldeyer ring, at the base of the tongue or in the salivary glands. The hard palate is the most common area for the development of a bone lesion.
- The most aggressive form of lymphoma is Burkitt lymphoma. The African form presents as a neoplastic growth in the head and neck area and is associated with EBV. The sporadic form usually presents as a mass in the abdomen and is less often associated with EBV.
- Leukemia refers to a diverse group of neoplastic disorders involving leukocytes. The acute forms of the disease exhibit symptoms very early in the disease process; the chronic forms progress more slowly.
- Immune suppression is a characteristic feature of all forms of leukemia because the white cells produced do not function correctly. Often, the first sign of a problem is an unexplained gingival infection accompanied by excessive gingival bleeding and gingival enlargement.
- The Philadelphia chromosome is present in most cases of chronic myelogenous leukemia (CML).
- Multiple myeloma is a malignant neoplasm of B lymphocytes, usually caused by an accumulation of genetic defects within the cells. The disease is associated with severe immunosuppression, bone resorption, and kidney failure.
- Extramedullary plasmacytomas are found in the soft tissues and may frequently be found in the oral cavity.
- Severe loss of blood from injuries is prevented by the process of hemostasis (coagulation). Platelets and the coagulation factors (produced in the liver) act together to maintain hemostasis. The process of coagulation centers on the coagulation cascade.
- Bleeding disorders are seen when there are too few or defective platelets or inadequate or defective coagulation factors.
- Severe hemophilia presents with hemarthrosis, hematuria, and bleeding into the muscles and gastrointestinal tract. Cerebral hemorrhage is also common in more severe cases. Intraoral findings include spontaneous gingival hemorrhage, petechiae, and ecchymoses.
- Dental management of a bleeding disorder focuses on preventing excessive blood loss and maintaining healthy oral tissues to decrease inflammation.
- An inadequate number of platelets or defective platelets presents as thrombocytopenia. Idiopathic thrombocytopenia purpura is caused by an autoimmune reaction that destroys the platelets.
- Nonthrombocytopenic purpura is associated with structurally weak vessel walls or damage due to inflammation or immune system disorders.

CHAPTER REVIEW

Case Study 9.1

Kristina Mendoza is 17 years old and about to leave home for her first semester of college. Her mother insisted she have a dental checkup before leaving for school. Her medical history is unremarkable except for a 10-lb weight loss since her last visit 6 months ago and high levels of anxiety associated with leaving home for college. During your intraoral examination you note the lesion seen in Figure 9.27.

1. The following list might be the differential diagnosis you would consider for this lesion. Using facts from the case or lack of them, rule out as many of the following conditions as possible.
   - Aplastic anemia
   - Leukemia
   - von Willebrand disease
   - Vitamin K deficiency
   - Thrombocytopenia
   - Anticoagulant medications
   - Trauma

FIGURE 9.27.

For answers and additional review activities, log in to **thePoint.lww.com**

Case Study 9.2

One of your favorite patients has brought his wife along with him to your dental hygiene clinic for an oral cancer examination while he is having periodontal debridement. She is 69 years old, edentulous, and wears full upper and lower dentures. Her main complaint is that her dentures have been difficult to wear lately. Her medical history is unremarkable except for stage 1 hypertension, treated with a diuretic, and a recent history of heart palpitations. Figure 9.28 shows what you see before you even start your intraoral examination.

1. What is the most striking observation?
2. What else do you see?
3. What type of follow-up questions do you want to ask?
4. What conditions do you want to include in a differential diagnosis?
5. Can you determine the cause of this condition without any more information? What additional information might be necessary?
6. What would be the outcome of this visit?

FIGURE 9.28. From Neville B, et al. Color atlas of clinical oral pathology. Philadelphia: Lea & Febiger, 1991, with permission.

For answers and additional review activities, log in to **thePoint.lww.com**

Critical Thinking Activities

1. List several obstacles you think might cause someone with a bleeding disorder to avoid receiving routine dental care. Look at your list, and using information from any available source and your imagination, develop strategies to overcome these obstacles. Share these with your classmates.
2. Examine your school's medical/dental history form and identify items that pertain to blood or bleeding disorders. Write down questions you would ask to get the most complete information from your patients.

Portfolio Possibilities

- Contact a community group in your area that provides education and support for patients who have hemophilia, sickle cell anemia, or thalassemia. Tell them you are a dental hygiene student and ask if you can present a short oral health program focused on maintaining healthy oral tissues and addressing the dental problems associated with that particular condition to some of their members. You might be able to survey some members to see if they have any specific oral health questions that you could help them find answers to. When you present your program, make sure that you ask questions about the participant's dental experiences, both good and bad. After your visit, write a summary of your experience with reflections on the information that you received from the individuals with whom you spoke. Include how some of their bad experiences might have been changed

into good experiences and how the good experiences might have been made even better. The following are good places to start looking for a community group:

- National Hemophilia Foundation: *http://www.hemophilia.org*; select the Chapter Center
- Sickle Cell Disease Association of America: *http://www.sicklecelldisease.org;* go to Member Organizations
- Cooley's Anemia Foundation: *http://www.thalassemia.org;* click on Chapters

Media Menu

Web Sites

Canadian Hemophilia Society
http://www.hemophilia.ca/en/

Sickle Cell Information Center
http://scinfo.org/

There for You: Your Online Hemophilia Resource—excellent site for health care providers and patients that includes specific dental information
http://www.thereforyou.com/managing-hemophilia/dental-care/

Multimedia Resource

National Hemophilia Foundation: Cell Based Coagulation Animation—excellent animation of clotting and use of clotting factors
http://www.hemophilia.org/NHFWeb/MainPgs/MainNHF.aspx?menuid=301&contentid=669&rptname=Research

Study Tools

Take advantage of additional online resources to help you study and ace your exams!

- Answers to case studies in the book
- Additional case studies and answers
- Interactive quiz bank with answer feedback
- Fully searchable e-book for quick lookup and studying on-the-go
- Expanded Media Menu with direct links to related Web sites and multimedia resources
- Supplemental references

thePoint Online resources and links are available at http://thepoint.lww.com/DeLong2e

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Chapter 9 **LESION/CONDITION SUMMARY TABLE**

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Hypochromic (iron deficiency) Anemia	Inadequate dietary intake, chronic blood loss, increased demand	Deficiency causes production of microcytic (small) red blood cells (RBCs) that are incapable of carrying the normal amount of O_2.	Tachycardia, dyspnea, weakness, fatigue, dizziness, pallor, brittle hair, nail changes (brittle, ridged, spoon shaped) Pale, atrophic mucosal tissues, glossitis, angular cheilitis, ulcers, burning sensations, dysphagia	Microcytic, pale (hypochromic) red blood cells	Identify etiology and correct, provide adequate dietary iron, eliminate source of chronic blood loss.	Review medical history and correlate with abnormal vital signs and oral findings; refer for medical evaluation if indicated Plummer-Vinson syndrome has an increased risk for esophageal and oropharyngeal cancers.
Thalassemia	Deletion or mutation of genetic material on chromosomes 11p and 16p	α–defects produce hemoglobin that will not release O_2. β–defects cause decreased production of hemoglobin and early destruction of cell.	α–most severe form incompatible with life, mutation of 1–3 genes causes moderate-to-negligible symptoms of general anemia β–Minor: few symptoms unless body is stressed by blood loss, inadequate iron intake, etc. Intermediate: mild-to-moderate general anemia. Major: severe anemia, bony malformations prominent maxilla and zygoma, anterior spacing, delayed eruption	Microcytic and hypochromic red blood cells Radiographic: honeycomb trabecular pattern, more radiolucent, "hair-on-end" effect in the skull	Treatment manages the mild-to-severe symptoms and ranges from no treatment to routine transfusions.	Patient may need prophylactic antibiotics if the spleen has been removed; establish coagulation status prior to treatment if taking anticoagulants, monitor occlusal problems and refer for orthodontic evaluation if necessary.
Pernicious Anemia	Autoimmune dysfunction stops the production of intrinsic factor so B_{12} is not transported across the intestinal mucosa. Dietary deficiency of B_{12} due to inadequate intake, malabsorption syndromes, alcoholism.	B_{12} is essential for synthesis of DNA and RNA causing the creation of large RBCs, which have a short life span requiring the bone marrow to produce more RBCs than normal, resulting in anemia. Deficiency causes peripheral nerve dysfunction as B_{12} is necessary to maintain myelin sheaths.	Fatigue, tachycardia, dyspnea, other general symptoms of anemia; blotchy or yellowed skin color; neurologic symptoms of paresthesia, loss of proprioception, ataxia Pale, ulcerated oral mucosa, glossitis with smooth "beefy red" color	Large abnormally shaped cells tend to rupture easily but carry the normal amount of hemoglobin.	Dietary supplements increased intake if deficient, treat malabsorption syndrome or other cause; lack of intrinsic factor requires routine administration of B_{12} by injection to bypass defective transport.	Careful review of medical history and correlation with abnormal vital signs and oral findings suggestive of B_{12} anemia indicate a referral for medical evaluation.
Folic Acid Deficiency Anemia	Inadequate dietary intake of folic acid	Folic acid is essential for synthesis of DNA and RNA causing a delay in the maturation of the red cell nucleus resulting in large RBCs, which have a short life span requiring the bone marrow to produce more than normal, resulting in anemia.	Fatigue, tachycardia, dyspnea, other general symptoms of anemia; blotchy or yellowed skin color Pale, ulcerated oral mucosa, glossitis with smooth "beefy red" color Associated with neural tube defects and possibly to cleft lip and palate if the mother is deficient during pregnancy	Large abnormally shaped cells tend to rupture easily but carry the normal amount of hemoglobin.	Increase dietary intake, dietary supplements, make sure women of childbearing age have adequate levels at all times.	Careful review of medical history and correlation with abnormal vital signs and oral findings suggestive of anemia indicate a referral for medical evaluation. Patient education regarding adequate levels of folic acid to help prevent neural tube birth defects and cleft lip and palate

continues

Chapter 9 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Sickle Cell Disease (SCD)	Autosomal recessive trait carried on chromosome 11p	Defective hemoglobin (HbS) causes cells to deform into sickle shape when exposed to hypoxia or dehydration; cells rupture easily, stick together, and lodge in vessels causing symptoms associated with chronic ischemia and sickle cell crises.	Fatigue, tachycardia, dyspnea, other general symptoms of anemia; jaundiced skin color from excessive loss or hemolysis of RBCs; damage to most organs related to infarcts; chronic pain, possible depression Crises include severe pain from multiple tissue infarctions	The Presence of RBCs in the characteristic sickled shape Radiographic: abnormal bone trabeculation and "hair-on-end" appearance of the skull	Manage symptoms with pain control, maintain adequate oxygenation and hydration; treat the complications related to organ damage; transfusions Stem cell transplants and gene therapy possible.	Patient education related to preventing oral infections to decrease risk of crises, stress consistent oral care; short appointments, supplemental oxygen, choose local anesthetics with little or no vasoconstrictors
Aplastic Anemia	Acquired (drugs, chemical, microbial or environmental agents) Congenital or inherited	Destruction or damage of the pluripotential stem cell resulting in decreased or no production of all blood cells	General signs of anemia, increased bleeding, increased infections, including severe oral and periodontal infections with spontaneous bleeding, petechiae, and ecchymoses	Lack of formed blood cells and platelets	Identify and eliminate cause of condition. Bone marrow transplants and immune suppression therapy	Careful review of medical history and correlation with abnormal vital signs; oral findings of anemia, bleeding, and infection indicate a referral for medical evaluation.
Polycythemia (primary and secondary)	Primary: proliferative neoplastic disorder of all cells Secondary: increase in RBCs due to chronic tissue hypoxia from anemia, cardiac and pulmonary disorders, high altitudes, smoking, some sports.	Primary: increase of all blood cells and platelets Secondary: red cells increase until tissue hypoxia is resolved and then stop.	Primary: increased blood volume, headaches, vision problems, reddening of skin and oral tissues, hypercoagulability, tissue infarcts, stroke Secondary: usually asymptomatic but may result in anemia if hypoxia is not reversed as in smoking and chronic diseases	Increased numbers of all cells or just RBCs	Primary: identify and eliminate cause, periodic phlebotomy, destruction of some bone marrow, myelosuppressive drug therapy. Secondary: no treatment identify and eliminate source of hypoxia if possible.	Careful review of medical history and correlation with oral signs of redness and excessive bleeding indicate a referral for medical evaluation.
Neutropenia, Agranulocytosis, Cyclic Neutropenia	Idiosyncratic or adverse reaction to a drug, genetic syndromes, autoimmune destruction, bone marrow neoplasms, anemia, chemotherapy drugs Cyclic: autosomal dominant inheritance	Numbers of circulating neutrophils are decreased due to decreased production, destruction, or loss of cells. Cyclic: recurring neutropenia every 21 days lasts for about 3 days then slowly returns to normal.	Fatigue, fever, malaise, weakness, abnormal vital signs, skin infections without exudate or erythema Severe, aggressive periodontitis is common; oral ulcerations. Cyclic neutropenia often results in premature loss of teeth.	Decreased numbers of neutrophils	Antibiotics to prevent infections, use of colony-stimulating drugs to increase the production of neutrophils	Focus on preventing oral infections to decrease risk of systemic infection and preventing/managing periodontal disease to preserve dentition; dental care should not be performed if neutrophil levels are too low, obtain a medical consult.

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Hodgkin Lymphoma	Unknown, risk factors may include infection with EBV or HIV genetic factors (higher risk in siblings).	Malignant transformation of B lymphocytes (Reed-Sternberg cell)	Asymmetric enlargement of one or more lymph nodes usually in upper body, significant weight loss, fever, drenching night sweats, fatigue, pruritus Unilateral enlargement of tonsils, submucosal swelling with or without ulceration	Presence of Reed-Sternberg cells Radiographic: erosion of underlying bone associated with intraoral lesions	Chemotherapy, radiation, monoclonal antibody therapy, bone marrow transplants, and stem cell transplants	Dental professionals may detect the initial enlarged lymph node while examining the patient during a routine dental visit; refer patients with enlarged nodes having no known etiologic factors for medical evaluation.
Non-Hodgkin Lymphoma	Unknown, chromosome changes especially translocations in chromosomes 18q, 11q, 14q, 12q, 1p	Genetic damage causes uncontrolled proliferation of abnormal B or T lymphocytes.	Lymphadenopathy (nontender and fixed) commonly affecting cervical, axial, and inguinal nodes first; fever, night sweats, weight loss are indicators of a poor prognosis. Oral manifestations uncommon but may appear as ulcerated or nonulcerated soft tissue masses in the tonsils and other lymph tissues, major and minor salivary glands, base of the tongue. HIV: oral lesions occur more commonly.	Radiographic: bone tumors can erode/perforate cortical bone causing tooth mobility, paresthesia, swelling, pain, and pathologic fracture.	Depends on type Most are radiosensitive and respond to radiation, chemotherapy, targeted therapy, and monoclonal antibodies.	Dental professionals may detect the initial enlarged lymph node while examining the patient during a routine dental visit, emphasizing the importance of performing a thorough head and neck evaluation; refer patients with enlarged nodes having no known etiologic factors for medical evaluation.
Burkitt Lymphoma	wSporadic form: little association with EBV (20%) Acquired immune deficiency syndrome (AIDS)	Possibly the most rapidly growing cancer known	Endemic: bony expansion of mandible or maxilla, loosening of teeth Sporadic: abdominal mass most common presentation AIDS: bone or soft tissue masses in the oral cavity common	Not applicable	Intense chemotherapy	Be aware of this condition especially if working with high-risk populations such as those with HIV infection or AIDS; refer any suspicious lesion for evaluation.
Leukemia (acute lymphocytic leukemia [ALL], acute myeloid leukemia [AML], chronic lymphocytic leukemia [CLL], chronic myeloid leukemia[CML])	Genetic damage or mutations; risk factors include exposure to chemicals, radiation, prior cancer chemotherapy.	Both acute and chronic cause very high numbers of abnormal, nonfunctioning cells resulting in increased blood viscosity, infiltration of tissues with excess WBCs; decreased production of RBCs, platelets, and nonaffected WBCs leading to anemia, neutropenia, and thrombocytopenia.	Acute: general symptoms of anemia, infection, night sweats, fever, bruising, epistaxis, petechiae, weight loss, bone pain, lymphadenopathy, nervous system disorders (ALL) Chronic: long-standing with mild or no symptoms; symptoms appear slowly: anemia, infections, excessive bleeding, lymphadenopathy, bone pain all point to progression of the disease; CML progresses through three stages (chronic, accelerated, acute). Oral findings include increased gingival/periodontal infection, bleeding, petechiae, purpura, and gingival enlargement more common in AML and CML.	Cellular appearance varies with type. Presence of the Philadelphia chromosome in most cases of CML and a few cases of ALL	Aggressive chemotherapy, monoclonal antibodies, targeted therapy focusing on cells containing the Philadelphia chromosome, stem cell transplants; supportive treatment: antibiotics, antifungals, antivirals, transfusions, medications to stimulate production of RBCs and neutrophils	Dental care is often sought prior to diagnosis because of the rapid decline in oral health, be vigilant to abrupt changes with no known cause; suspect systemic illness if infections do not respond to normal therapy, correlate to positive medical history findings such as fever, weight loss, etc. Provide elective care while WBC counts are adequate, consult with the physician to determine WBC levels and INR. Stress good oral hygiene practices.

continues

Chapter 9 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Multiple Myeloma	Acquired genetic mutations especially p53 (tumor suppressor gene); risk factors include radiation, age, obesity, and family history.	B-cell malignancy results in the overproduction of plasma cells, which results in immunosuppression, osteoclast activation, and production of Bence Jones protein.	Bone resorption, pathological fractures, pain, infections, renal failure due to accumulation of Bence Jones protein and hypercalcemia, bone lesions seen in both mandible and maxilla macroglossia; periodontal infections. Solitary plasmacytoma: single area of bone destruction (ribs, vertebrae, pelvis) Extramedullary plasmacytoma: soft tissue tumors seen mostly in the oral cavity and upper respiratory tract	Bone marrow samples with over 30% plasma cells Radiographic: multiple well-defined radiolucent "punched out" areas in the skull and jaws	Aggressive chemotherapy, radiation therapy for single or painful bone lesions; use of bisphosphonates or other osteoporosis drugs to strengthen bones and stimulate osteoblast activity; stem cell transplants	Focus on controlling infections; consult with physician to determine blood cell levels prior to treatment, watch medical history for the use of anticoagulant drugs or thrombocytopenia and determine INR if indicated; be aware of bisphosphonate use and educate the patient about osteonecrosis of the jaw and risk factors and stress prevention with adequate home care, etc.
Hemophilia A and B	X-linked recessive disorders	A: factor VIII deficiency B: factor IX (Christmas) deficiency Both result in defective or inadequate clot formation.	Excessive bleeding ranging from mild to severe and spontaneous, hemarthrosis, bleeding into muscles and GI tract, hematuria, heavy menstrual flow, heavy blood loss during childbirth (very high risk), intracranial hemorrhage, ecchymoses Minor-to-severe gingival bleeding depending on the type and severity of deficiency; excessive bleeding after trauma or dental surgery; ecchymoses	Not applicable	Replacement of the defective factor, use of desmopressin to stimulate release of factor VIII; avoiding use of medications associated with anticoagulation effects; modify activities to prevent injuries and hemarthrosis.	Consult with physician prior to treatment to obtain INR and other test results, discuss plan for hemostatic control during and after treatment; pretreatment need for factor replacement if anticipating mandibular block; consider use of tranexamic acid rinses and oral aminocaproic acid to enhance and maintain clots; avoid trauma if possible sutures may be necessary for even minor trauma; use antibiotic prophylaxis for total joint replacement. Patient education should stress prevention, identify and deal with barriers to care, discuss prevention of bacteremias.

Chapter 9 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
von Willebrand Disease	Autosomal dominant and recessive forms; acquired damage from aortic stenosis	Inadequate or defective von Willebrand factor causes inadequate or defective platelet adhesion to injured sites, may be an associated deficiency of factor VIII.	Usually mild and unnoticeable to moderate bleeding tendencies; but may have uncommon severe form and present with spontaneous hemorrhage, oral mucosal petechiae, and purpura	Not applicable	Replacement of the von Willebrand factor, use of desmopressin to stimulate release of factor VIII; avoiding use of medications associated with anticoagulation effects	Often the first manifestation of disease is seen with tooth extraction. Careful review of medical history and correlation with oral signs of excessive bleeding may indicate a need to refer for medical evaluation; any implication noted with hemophilia may be applied in von Willebrand disease. However, many of the above implications may not be appropriate in mild forms of disease, use judgment and medical consultation to determine correct action for each patient.
Thrombocytopenia (idiopathic thrombocytopenia purpura)	Platelet levels under 150,000/mm^3 blood; aplastic anemia, medications, radiation and chemotherapy, genetic, immune system dysfunction	Decreased production, ineffective production or destruction of platelets resulting in impaired platelet function and inadequate clot formation	Petechial hemorrhages in the skin of legs and feet, easy bruising, purpura, epistaxis, heavy menstrual flow, GI bleeding, retinal hemorrhages Gingival bleeding, petechial and hemorrhagic bulla of oral mucosa and lips	Increased numbers of megakaryocytes in bone marrow	Determine cause and eliminate or control. Immune disorders are treated with transfusions, steroids and intravenous immunoglobulin.	Identify excessive bleeding and refer to a physician for evaluation; use local hemostatic measures as indicated; determine platelet levels and coagulation status prior to treatment.

10 Respiratory, Gastrointestinal, Neurologic, and Skeletal Disorders

KEY TERMS

Abfraction
Atelectasis
Aura
Bradykinesia
Demyelination
Diverticula
Droplet nuclei
Dyskinesia
Emulsifier
Febrile
Hemoptysis
Hyperacusis
Hypercementosis
Nosocomial
Osteonecrosis
Osteophyte
Parafunctional
Paroxysm
Peristalsis

LEARNING OUTCOMES

1. Define and use the key terms in this chapter.
2. Describe how to limit the spread of the common cold and influenza within the dental office.
3. Discuss why antibiotics should not be used to treat the common cold or influenza.
4. Identify the medication associated with Reye syndrome and note those at highest risk for the syndrome.
5. Describe how dental biofilm may be cause ventilator-associated pneumonia.
6. Describe the dental management of an individual suspected of having tuberculosis.
7. Identify the type of personal protective equipment and environmental controls that need to be available for the dental professional to safely treat an individual with active tuberculosis.
8. Identify common triggers for asthma attacks and describe symptoms associated with an attack.
9. Describe treatment options and the dental implications of asthma.
10. Compare and contrast the clinical characteristics of emphysema and chronic obstructive bronchitis.
11. Describe the dental implications of COPD
12. Describe the extraoral, perioral, and intraoral manifestations of cystic fibrosis.
13. Identify the dental implications of cystic fibrosis.
14. Discuss the difficulties associated with dysphagia.
15. Discuss the dental implications of GERD and describe recommendations to prevent dental problems.
16. Identify the most common etiologic agents for peptic ulcers.
17. Describe how malabsorption syndromes cause vitamin and mineral deficiencies.
18. Identify oral manifestations associated with celiac disease.
19. Identify oral manifestations associated with Crohn disease.
20. Describe the characteristic oral and perioral lesions seen in Peutz-Jeghers syndrome.
21. Identify the gastrointestinal disorders associated with an increased risk of cancer.
22. Identify special population groups at high risk for meningococcal disease.
23. Describe clinical symptoms common to both encephalitis and meningitis.
24. Describe the physical characteristics and typical oral problems associated with Parkinson disease.
25. Identify etiologic agents associated with Bell palsy.
26. Describe clinical manifestations and dental implications associated with Bell palsy.
27. Describe trigeminal neuralgia and identify a suspected etiology.
28. List oral manifestations associated with migraine headache.
29. Describe burning mouth syndrome and list elements that would be included in a differential diagnosis.
30. Compare and contrast osteoarthritis and rheumatoid arthritis.
31. Describe the dental implications of osteoarthritis and rheumatoid arthritis.
32. List risk factors for osteoporosis and osteopenia and describe the dental implications.
33. Describe the extraoral, perioral, and intraoral characteristics of Paget disease.
34. Identify the element that is always significantly elevated in the blood of individuals with Paget disease.
35. Identify the characteristic radiographic finding in Paget disease.
36. Identify and describe the characteristics of the different forms of fibrous dysplasia.
37. Identify the etiology of cherubism.
38. Describe the perioral, oral, and radiographic findings characteristic of cherubism.
39. Describe antiresorptive drug-induced osteonecrosis and the factors associated with an increased risk of ARONJ.
40. Describe methods to identify and manage the patient with a temporomandibular joint disorder.

CHAPTER OUTLINE

Respiratory System Disorders
- Upper Respiratory Diseases
  - Common cold
  - Influenza
  - Reye syndrome
- Lower Respiratory Diseases
  - Pneumonia
  - Tuberculosis
- Obstructive Pulmonary Diseases
  - Asthma
  - Chronic obstructive pulmonary disease
  - Cystic fibrosis

Gastrointestinal System Disorders
- Dysphagia
- Gastroesophageal reflux disease
- Peptic ulcer
- Crohn disease
- Peutz-Jeghers syndrome
- Malabsorption syndromes
  - Celiac disease

Nervous System Disorders
- Meningitis and encephalitis
- Parkinson disease
- Bell palsy
- Trigeminal neuralgia
- Migraine headache
- Burning mouth syndrome

Skeletal System Disorders
- Osteoarthritis
- Rheumatoid arthritis
- Osteoporosis
- Paget disease
- Fibrous dysplasia
- Temporomandibular Joint Disorders
  - Temporomandibular disorder

RELATED CLINICAL PROTOCOLS

#4 Treating Patients with Xerostomia
#5 Diagnosing and Treating Patients with *Candida*
#8 Treating Patients with Intraoral Ulcers
#25 How to Utilize Nutrition Counseling in Practice

Important concepts of general pathology have been discussed throughout the earlier chapters in this text; however, some additional medical disorders need to be reviewed to help prepare students to safely provide appropriate patient treatment. This chapter discusses pertinent information and dental implications related to these conditions.

Respiratory System Disorders

The respiratory system consists of structures that bring air into the lungs, transfer oxygen into the bloodstream, and allow the lungs to expand and contract. The nasal cavity, oral cavity, larynx, pharynx, trachea, bronchi, and bronchioles bring air from the environment into the lungs. Oxygen is exchanged for carbon dioxide in the alveoli. The diaphragm and the external intercostals are the muscles of inspiration. When these muscles contract, the volume of the chest cavity increases, and outside air enters the lung. The rate of contraction is regulated by the respiratory center in the medulla of the brain, which senses carbon dioxide levels in the blood and stimulates the muscles of inspiration to contract. Air leaves the lungs when these muscles relax. The abdominal and internal intercostal muscles assist with expiration, if necessary, as in emphysema. The lungs are enclosed by the pleura, a double membrane separated by the pleural cavity, which is filled with a special fluid that lubricates the lungs as they expand and contract. The respiratory tract is lined with specialized respiratory epithelium containing cilia that help to prevent foreign objects or substances from entering the lungs.

The respiratory system is divided into the upper respiratory tract, which consists of the structures of the nose and throat, and the lower respiratory tract, which comprises the trachea, bronchi, and lungs.

Upper Respiratory Diseases

Upper respiratory diseases are among the most common infections known to man and cause significant amounts of time away from school and work each year. The common cold and influenza are examples of upper respiratory diseases.

NAME: Common cold

Etiology: The common cold is an acute inflammation of the mucous membrane lining of the upper respiratory tract. The viruses most often associated with the common cold are rhinoviruses (110 different types) and coronaviruses, among others (DePaola, 2011).

Method of Transmission: Although these viruses can be transmitted through the air and inhaled, transmission by hands and fingers contaminated with the virus is more likely to occur. As few as 1 to 30 viral particles have been known to cause an infection (DePaola, 2011).

Epidemiology: About one billion of these infections occur every year in the United States alone. Adults average two to four infections per year, while children may have as many as ten infections per year (DePaola, 2011).

Pathogenesis: Symptoms of the infection occur within 10 to 12 hours after the virus is introduced to the nasal mucosa. The first symptom is usually a sore throat, followed by congestion, initially caused by inflammation and swelling of the membranes and narrowing of the nasal passageways, and nasal discharge caused by secretion of copious amounts of mucus by the inflamed glands. Viral-induced mucosal secretions are clear and watery. The altered environment of the nasal passages and compromised immune

APPLICATION **10.1**

Preventing Colds/Flu

The best treatment for colds and flu is to try to prevent them. While exposure to infectious organisms cannot be eliminated, there are many ways to limit exposure to these organisms. The following are some strategies to help prevent the spread of both colds and flu in the dental office and beyond.

- Perform frequent hand hygiene (washing). This is probably the most effective weapon available for preventing the spread of these and other infections. Hand hygiene should be performed after any patient contact or contact with surfaces that are potentially contaminated with respiratory secretions.
- Use a preoperative antimicrobial mouth rinse to limit the microorganisms that could be aerosolized during a dental procedure.
- Place dispensers of alcohol-based hand rub or towelettes for patient use where sinks are not available, such as in the reception room.
- Encourage dental health care workers to remain at home if they have flu or cold symptoms.
- Make sure all dental health care workers receive a flu vaccination if appropriate and available.
- Disinfect as much of the reception room furniture as possible. Disinfect toys and discard any toy that cannot be disinfected.
- Encourage everyone to cover their nose and mouth with tissues when coughing or sneezing. Tissues and receptacles for contaminated tissues should be placed throughout the office.
- Keep a mask on when working with a patient who may have a cold or the flu and leave it on after the patient has left the room and during cleanup.
- Avoid close contact with sick people.
- Reschedule sick patients (should be fever free for at least 24 hours without fever-reducing drugs).
- Perform hand hygiene prior to eating or touching your mouth, nose, or eyes.
- Avoid casual hand contact with the public (shaking hands, etc.).
- Take advantage of alcohol hand rub stations scattered throughout public areas.

For more information, visit: http://www.cdc.gov/pertussis/about/prevention.html

status predispose the individual to superinfection or coinfection by pyogenic bacterial organisms as evidenced by the production of thick, yellow or green mucous secretions occurring within days of the initial symptoms. The offending bacterial organisms are usually streptococci, staphylococci, or pneumococci.

Extraoral Characteristics: Symptoms usually include sinus congestion, profuse nasal discharge, fatigue, malaise, myalgia (muscle pains), headache, and hoarseness. Fever is frequently present in children but not adults.

Perioral and Intraoral Characteristics: A sore, scratchy throat is often the first symptom of an impending cold.

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: Appropriate hand hygiene and maintaining standard precautions at all times are essential for reducing or eliminating the chance of spreading these viruses to others. Dental health care professionals should avoid direct patient care when they have a cold.

Differential Diagnosis: Not applicable

Treatment and Prognosis: There is no cure for the common cold, which resolves on its own in 7 to 11 days. Supportive treatment includes rest and adequate hydration. There is no need for antibiotic medications unless there is a concomitant bacterial infection, a rare sequela. It was common medical practice in the past to prescribe antibiotics for individuals with a cold, not to treat the cold, which is viral, but to prevent a bacterial coinfection. This practice is no longer considered appropriate because of the risk of creating antibiotic-resistant organisms. Medications that alleviate symptoms associated with colds include decongestants, cough suppressants or antitussives, and expectorants, which help to loosen and remove mucus from the respiratory tract. Nasal sprays or drops should be used only when necessary because continued use over more than 3 days can cause rebound congestion when the drug is withdrawn.

NAME: Influenza

Etiology: Influenza can affect both the upper and lower respiratory tracts and is caused by influenza virus types A, B, and C. The influenza viruses are known for their ability to mutate into new and often more virulent strains. Every mutation requires the development of a new vaccine to stop the spread of the disease; consequently, new vaccines need to be produced every year to combat the newest forms of the virus. This also explains why people who have the flu 1 year are not immune to the flu the next year.

Method of Transmission: The virus is transmitted to an uninfected host's oral or nasal mucous membranes through inhalation of aerosols containing the organism (created when an infected person coughs, sneezes, or speaks) or through contact with contaminated objects.

Epidemiology: Influenza occurs in epidemic or pandemic (worldwide) proportions causing more than 500,000 deaths every year (DePaola, 2011). Influenza is a known killer, with most deaths occurring in the elderly and the very young. The 2009 pandemic outbreak of influenza A H1N1 (swine flu)

found most victims under the age of 25 with 30% of those infected shown to be previously strong and healthy.

Pathogenesis: There is a short incubation period of up to 3 days, and viral shedding (the ability to spread the virus) occurs from 0 to 24 hours before symptoms arise until 5 to 10 days after. Children and severely immunocompromised individuals may shed the virus for weeks or months (Derlet et al., 2011). The copious nasal discharge associated with the flu is caused by necrosis and shedding of serous and ciliated cells lining the respiratory tract allowing fluid to escape from the tissues. Gastrointestinal (GI) symptoms of diarrhea and nausea occur in about 10% of cases (Porth, 2011). The infection is normally self-limiting, with symptoms resolving in 7 to 10 days. However, the greatest danger associated with influenza is its ability to cause more severe infections in high-risk individuals, such as the very young, the elderly, those with preexisting cardiac or pulmonary disorders, and the immunocompromised. Viral pneumonia and/or a bacterial coinfection can cause death from respiratory failure in just days.

Extraoral Characteristics: Early symptoms of influenza include fever, headache, and rapid onset of profound malaise.

Perioral and Intraoral Characteristics: Malaise is followed closely by sore throat and cough.

Distinguishing Characteristics: Rapidly occurring profound malaise, sometimes within minutes, is characteristic of this infection.

Significant Microscopic Features: Not applicable

Dental Implications: All health care workers should receive an annual influenza vaccination unless contraindicated in specific instances. Appropriate hand hygiene and maintaining standard precautions at all times are essential for reducing or eliminating the chance of spreading these viruses to others. Dental health care professionals should avoid direct patient care when they have influenza. Patients with influenza should not be treated until they no longer have a fever and are feeling well enough to withstand treatment.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment depends on quick and accurate diagnosis. Many physicians are offering rapid diagnostic testing, which can determine the etiologic nature of flu-like symptoms within 30 minutes or less (Derlet et al., 2011). Antiviral medications are available to help prevent the flu and also to treat the infection in individuals who have been diagnosed with influenza. These drugs can shorten the duration of symptoms by an average of 1.5 days when given within 36 to 48 hours of the onset of symptoms, decrease the potential for transmitting the virus, and decrease the severity of the symptoms. Zanamivir (Relenza) and oseltamivir (Tamiflu) are second-generation antiviral drugs with less chance of creating resistance and fewer side effects than the first-generation antivirals. Zanamivir is administered intranasally and should not be used in those with some pulmonary disorders because it may cause bronchospasms (Porth, 2011). Supportive measures focus on rest, hydration, keeping warm, and staying away from others to whom the virus can be transmitted. Antipyretics can lower fevers, but the use of aspirin or aspirin-containing medications should be avoided in children because of the risk of Reye syndrome.

Reye Syndrome

In the early 1960s, several physicians observed a distinct set of symptoms that seemed to occur following a viral illness that had been treated with aspirin. Reye syndrome was named after the Australian physician who first recognized it. The etiology and pathogenesis of Reye syndrome are obscure. However, Reye syndrome is associated with the use of aspirin or aspirin-containing products to treat the symptoms of influenza and several other **febrile** (fever producing) diseases of viral etiology in young children. Reye syndrome consists of liver and kidney damage, and brain pathology associated with edema from inflammatory exudates leading to brain damage, coma, and death. Because of the potential for this syndrome, it has become standard practice to never prescribe or give aspirin or aspirin-containing products to children, especially those who have colds or other febrile illnesses (Weiner, 2011).

Lower Respiratory Diseases

Lower respiratory tract diseases are usually more severe and are often chronic, unlike upper respiratory diseases. Disorders of the lower respiratory tract include pneumonia, tuberculosis (TB), and obstructive airway disorders, specifically, asthma, chronic obstructive pulmonary disease (COPD), and cystic fibrosis (CF), as well as others.

NAME: Pneumonia

Etiology: Pneumonia can be defined as an inflammation of the bronchioles and the alveoli within the lungs. Most cases are caused by bacteria or viruses, but fungal infections, inhalation of toxic fumes, and aspiration of substances, such as vomitus, or microbes, such as those associated with dental biofilm, are not infrequent causes of pneumonia.

Method of Transmission: Bacterial and viral pneumonia are transmitted through inhalation of contaminated aerosols or through inoculation of the respiratory mucosa by contaminated hands, fingers, or other objects. Transmission of pneumonia is categorized into the following two types:

- Community-acquired pneumonia, which is not contracted in a hospital or long-term care facility
- **Nosocomial** pneumonia, which is contracted within a hospital or long-term care facility by susceptible individuals. This includes ventilator-associated pneumonia (VAP) that occurs in 9 to 27% of intubated patients (Kamangar et al., 2012).

APPLICATION **10.2**

The Resurgence of Whooping Cough (Pertussis)

Pertussis is a highly contagious bacterial infection, *Bordetella pertussis*, which first appears with symptoms of a common cold that last from 1 to 2 weeks. The symptoms progressively worsen during the next 2 to 6 weeks (or longer) with paroxysms or multiple fits of rapid coughing followed by a "whooping" sound as the patient tries to inhale through swollen and spastic airways. Recovery takes many weeks and coughing fits may recur for months. Pertussis affects all ages but is especially serious in infants. Pertussis was a major cause of death in infants and children from medieval times up until the 1940s when a vaccine against *B. pertussis* was developed and combined with the tetanus and diphtheria vaccination (DTP). At that time, reported cases of pertussis dropped 99% and remained low until the 1980s when cases began to rise dramatically across all age groups (2008:13,278 cases; 2009:16,858 cases) with the largest increases found among adolescents and adults. Between 2001 and 2003, infants younger than 1 year accounted for 23% of cases, adolescents aged 10 to 19, 33%; and adults over the age of 20, 23%. Because vaccine protection against pertussis fades over time, the CDC has mounted a public awareness campaign about the revised immunization schedules for most groups. There are two types of vaccine available: diphtheria, tetanus, and acellular pertussis (DTaP), which is given to children and infants ages 6 and under, and tetanus, diphtheria, and pertussis (Tdap), which is given to those over the age of 6. The major emphasis is on reimmunizing adolescents and adults who have not received the new acellular pertussis vaccination in combination with the DTP. Major revisions in the vaccination recommendations for adolescents and adults are outlined below:

- A dose of Tdap is recommended at age 11 or 12.
- Adults aged 19 to 65 should have one booster dose of Tdap in place of the tetanus and diphtheria (Td) vaccination at their next scheduled booster vaccination.
- Adults over the age of 65 may get one dose of Tdap at their next scheduled Td vaccination.
- Any adult or adolescent (including women who may become pregnant) who has not yet had a dose of Tdap and anticipates or has close contact with an infant under the age of 1 year should have a dose of Tdap as soon as possible (even if a regular Td vaccination is not required yet) to help protect the infant from pertussis.
- Pregnant women who have not had a dose of Tdap should be vaccinated after the 20th week of gestation. Maternal circulation may provide enough antibodies to help protect the infant after birth until the immune system develops more.
- Health care workers who have direct patient contact should have one dose of Tdap as soon as possible if they have not had one before (even if a regular Td vaccination is not required yet).

For more information, visit: http://www.cdc.gov/pertussis/about/prevention.html

Other factors associated with an increased risk for pneumonia include altered levels of consciousness that impair the ability to gag or to clear the lungs by coughing, esophageal dysfunction leading to aspiration of matter into the lungs, neurologic disorders such as dementia, and mechanical intrusions into the body such as intubation for ventilation or endoscopic examination of the esophagus or lungs. Current research shows a relationship between VAP and chronic gingivitis or periodontitis and may lead to the establishment of oral care protocols for health care workers who care for these patients (Mojon, 2002; Gomes-Filho et al., 2010).

Epidemiology: Approximately 3 million cases of pneumonia occur in the United States each year (Kamangar et al., 2012). Males are diagnosed with pneumonia more often than females, and the elderly are affected more often than younger individuals. Individuals with preexisting pulmonary conditions, smokers, and those who are immunocompromised are at the highest risk of developing pneumonia.

Pathogenesis: The specific pathogenesis depends on the cause of the pneumonia with all causing an inflammatory response within the lung resulting in the production of exudate that obstructs air spaces within the lung, preventing exchange of gases that normally occurs in these areas.

Extraoral Characteristics: Symptoms of pneumonia include fever, dyspnea, productive cough (cough that brings up sputum), tachycardia, weakness, anorexia, and chest pain.

Perioral and Intraoral Characteristics: Not applicable

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: Oral bacteria in dental biofilm can be aspirated into the lungs and cause pneumonia. Several studies have reported up to a 50% reduction in the rate of pneumonia in hospital patients who have daily mechanical removal of dental biofilm with or without antibacterial rinses (Teng et al., 2002). While most studies exploring this relationship were conducted in hospitals or long-term care facilities, the information can be applied to situations where debilitated patients are being cared for in the home and to anyone with a respiratory disorder. Dental hygienists have an excellent opportunity to provide this information during patient visits and during community education programs.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Both the treatment and prognosis depend on the cause of the pneumonia and the immune status of the host. All forms are treated with supportive therapy as needed, including adequate hydration, nutrition,

supplemental oxygen, and mechanically assisted ventilation, if required. Bacterial pneumonia, including aspiration pneumonia, is treated with antibiotics. Viral pneumonia is sometimes treated with antivirals, depending on the specific risks involved and the general health of the individual. Chemical aspiration pneumonia is usually treated by removal of the offending agent, if possible, and with supportive oxygen therapy. Most individuals will recover from pneumonia; however, those with preexisting respiratory disorders often see a worsening of the underlying condition and may be subject to frequent recurrences of pneumonia. Data for mortality rates are specific for the type of pneumonia, but in all cases, the elderly have the highest mortality rates. Prevention is possible through strict adherence to standard precautions and through vaccination for one of the more common bacterial pneumonias, pneumococcal pneumonia, which is recommended for individuals over the age of 65, those with a compromised immune system, those with chronic illness, and residents of long-term care facilities.

NAME: Tuberculosis

Etiology: *Mycobacterium tuberculosis* is the etiologic agent associated with TB. Most of these organisms are susceptible to the drugs commonly used to treat an infection with them. However, drug-resistant forms of the bacterium have developed and infections with the resistant forms are classified as either multidrug-resistant (MDR) or extensively drug-resistant (XDR). MDR strains are resistant to two of the first-line drugs, isoniazid and rifampin, and XDR strains are resistant to both of these plus at least one of the second-line drugs (CDC, June 20, 2011). Resistant strains of *M. tuberculosis* have developed as a result of inappropriate drug therapy, (length of time, amount of dose, type or quality of drug) or incomplete or early discontinuation of treatment, the latter usually because of patient noncompliance with the treatment regimen.

Method of Transmission: TB is spread through inhalation of **droplet nuclei,** microscopic particles containing the *M. tuberculosis* organism. Transmission depends on the number of bacilli that are inhaled, the environment from which they are inhaled, the duration of the exposure, and the virulence of the organism.

Epidemiology: In the early to middle 1980s, after years of a steady decline in TB, there was an increase in the number of cases of TB in the United States. This increase was attributed to the human immunodeficiency virus (HIV) epidemic, the increase in the number of immigrants from areas that had endemic TB, outbreaks in institutional settings, and the emergence of drug-resistant forms of the bacterium. This increase continued until 1993, when the number of cases again started to drop. The Center for Disease Control and Prevention's (CDC) most current data show that the 2010 TB rate of 11,182 new cases is the lowest reported since national TB data started being collected in 1953 (CDC, October 19, 2011). The numbers of MDR cases have decreased since 1993 when they were first reported and represent 1.2% of cases in 2010. XDR cases are rare in the United States with only 83 cases being reported between 1993 and 2007 (Shah et al., 2008).

Factors associated with an increased risk of acquiring TB infection are listed in Box 10.1.

BOX 10.1 Risk Factors for Infection with *Mycobacterium Tuberculosis*

- Close contacts of persons with known TB infection
- Infants, children, and adolescents exposed to high-risk adults
- Foreign-born individuals from areas in which TB is endemic
- Residents and employees of long-term care facilities or other such institutions that provide living arrangements for extended periods of time
- Medically indigent and low-income groups
- Substance abusers, especially injection drug users
- Health care workers involved with high-risk populations

Pathogenesis: After the organisms have been inhaled, they are carried into the alveoli, where they are surrounded by macrophages and ingested. Most of the bacilli are destroyed, but some may survive within the macrophages, begin to multiply, and are eventually released when the macrophage dies. The immune system is activated by macrophages when the ingested antigen, the TB bacterium, is presented, thereby initiating a cell-mediated immune response against the organism. The immune response is usually a localized inflammatory reaction in which the *M. tuberculosis* is surrounded by more macrophages and other white blood cells, creating a granuloma or tubercle. The tissues within the tubercle undergo caseous necrosis (see Chapter 2), and the entire area becomes surrounded by fibrous scar tissue, effectively isolating any remaining *M. tuberculosis*. At this point, the infection is contained, and the person is said to have latent TB infection (LTBI). Some 90% of individuals with healthy immune systems who are exposed to *M. tuberculosis* remain in this status for the rest of their lives. They do not have active TB infection, and they are not infectious nor can they spread the disease (CDC, June 20, 2011). They will, however, have positive Mantoux skin test results for the rest of their lives, due to a type 4 delayed hypersensitivity reaction (see Chapter 4) to the antigen, TB bacterium.

Approximately 5 to 10% of individuals will progress to TB disease; most of these will occur within 2 years of the original infection and the rest may occur many years later. TB disease can result from either a reactivation of the original infection or exposure to a second infection. Reactivation of the original infection is most often due to a change in the immune status of the individual, such as the use of immunosuppressive drugs, infection with HIV, diabetes mellitus, head and neck cancer, end-stage renal disease, malnourishment, and intravenous substance abuse. TB disease differs from LTBI because this time the immune response causes many tubercles to form, resulting in tissue destruction by

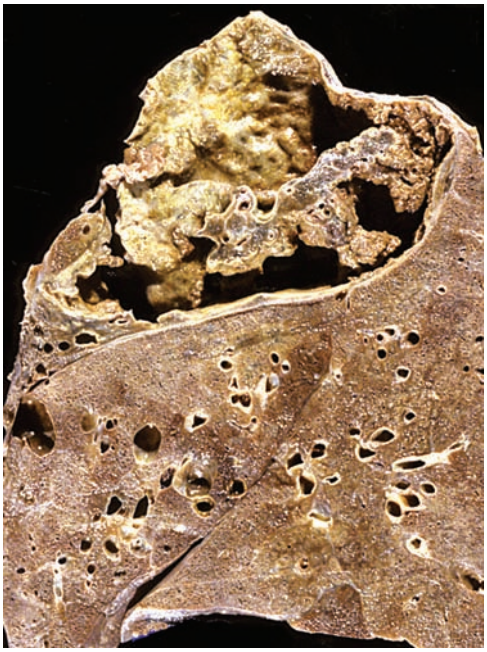

FIGURE 10.1. Tuberculosis (TB disease). This example of TB disease shows the formation of a necrotic cavity involving the entire upper lobe. Involvement of any of the blood vessels, as was very likely, would have caused bleeding into the lung and hemoptysis. (From Cagle PT. Color atlas and text of pulmonary pathology. Philadelphia: Lippincott Williams & Wilkins, 2005.)

both the infection and the hypersensitivity reaction caused by the bacteria. Large cystic areas, or cavities, up to 10 cm in diameter may form within the lungs (Fig. 10.1), where they often compromise or break through into a bronchus, releasing the contents of the cavity into the lungs and causing the individual to cough up infected sputum. Lung collapse, **atelectasis,** can result if the formation of tubercles compromises the pleural cavity, and **hemoptysis,** blood in the sputum, results if a pulmonary blood vessel is destroyed causing bleeding into the lungs. Blood vessel involvement and involvement of the lymphatic system can result in circulation of TB throughout the body and infection of any organ or body part. This rare diffuse extrapulmonary form of TB disease is called miliary TB, or disseminated TB, and most commonly affects the lungs, lymph nodes, kidneys, spleen, and liver.

Extraoral Characteristics: LTBI is usually asymptomatic, with most individuals only becoming aware of its presence when they have a positive Mantoux skin test. A positive test result should be followed by a chest x-ray to determine the presence of lung lesions. The final diagnosis is made by bacteriologic or histologic examination of the sputum, if present. The symptoms associated with TB disease are afternoon fevers, night sweats, weight loss, weakness, chest pain, a productive cough (sputum), and hemoptysis.

Perioral and Intraoral Characteristics: Oral lesions usually develop secondary to a primary lung infection and are caused by implantation of infected sputum into a break in the mucosal surface during coughing episodes. Oral TB lesions appear as painful nonhealing ulcers found most often on the tongue, although they can be found on any mucosal surface (Fig. 10.2).

FIGURE 10.2. Oral tuberculosis ulcer. This oral ulcer is caused by implantation of *M. tuberculosis* from an already present lung infection in compromised oral mucosa. (Courtesy of the U.S. Department of Veteran's Affairs.)

Distinguishing Characteristics: Chronic productive cough with associated weight loss, night sweats, and hemoptysis is characteristic of TB disease.

Significant Microscopic Features: The presence of acid-fast bacilli (AFB) in a stained sputum smear shows infection with a mycobacterial species; further testing to determine the exact type (*M. tuberculosis*) has to be done.

Dental Implications: Dental professionals need to be aware of the potential for the spread of TB within the dental office environment. Office protocols should be in place to enable prompt detection of suspected cases, isolation of infectious patients, and referral for appropriate treatment. Persons with TB disease should not be treated in dental facilities without proper air treatment capabilities including an effective ventilation system containing high-efficiency particulate air (HEPA) filtration and ultraviolet germicidal irradiation (UVGI). Health care workers should use personal respirators effective at the N-95 particulate level in instances when air filtration and irradiation are not in use. Precautions to prevent the production of airborne particles should also be used, for example, using high-volume evacuation during emergency treatment. See Box 10.2 for criterion used to assess the infectious status of the patient who reports a recent positive history of TB.

Differential Diagnosis: Not applicable

Treatment and Prognosis: LTBI is usually treated with isoniazid and rifampin using one of several different regimens lasting from 3 to 9 months of total treatment. The newest regimen announced in the latter part of 2011 is considered a significant breakthrough by some because it involves one weekly dose of combined isoniazid and rifampin for

BOX 10.2

Criteria for Determining Noninfectious TB Status

Patients can be considered noninfectious when they meet all of the following three criteria:

1. Three consecutive negative acid-fast bacilli (AFB) sputum smears collected in 8- to 24-hour intervals (at least one early morning)
2. Symptoms have improved clinically (coughing less, no fever)
3. Compliant with an adequate treatment regimen for 2 weeks or longer

BOX 10.3

Triggers Associated with the Initiation of an Asthma Attack

- Lung infections (colds)
- Tobacco smoke
- Allergies (molds, pollen, animals, etc.)
- Exercise
- Cold air
- Excitement
- Stress
- Drugs (aspirin)
- Air pollution

12 weeks (3 months). Studies have shown this regimen to eliminate the organism and prevent TB disease as well as the longer regimens in otherwise healthy patients with a higher rate of compliance (CDC, January 20, 2012). TB disease is treated with a combination of drugs to which the organism is susceptible in an effort to prevent the development of more resistant strains. The treatment regimen recommended for most individuals contains four drugs: (1) isoniazid, (2) rifampin, (3) pyrazinamide, and (4) ethambutol. The drugs are usually given for 6 to 9 months. Since the major variable in the outcome of drug therapy and the development of MDR and XDR TB is patient compliance, adherence to treatment regimens is always stressed. However, drug abusers, homeless persons, individuals with mental health issues, and others in the highest-risk population groups are not always the most reliable when it comes to being responsible for taking medications appropriately.

Therefore, both LTBI and TB disease treatment regimens rely heavily on directly observed therapy or DOT to monitor all individuals who are under treatment for LTBI or TB disease.

In the absence of complications, the prognosis for most individuals is good. The immune status of the host and the susceptibility of the organism to the medications currently available are significant factors in the determination of an individual's prognosis. The CDC reported 547 TB-related deaths in 2009 (CDC, October 19, 2011). MDR and XDR TB present more difficult treatment problems and have poorer prognoses especially in immunocompromised individuals.

Obstructive Pulmonary Diseases

Obstructive pulmonary diseases are associated with either chronic or episodic airway obstruction in which difficult expiration or exhalation of air is the major presenting feature. Asthma, emphysema, chronic obstructive bronchitis, and CF, among others, are considered to be obstructive pulmonary diseases.

NAME: Asthma

Etiology: The etiology of asthma is mostly unknown. Generally, asthma is caused by an inflammatory reaction within the bronchial airways caused by excessive sensitivity of the mucosal membranes and muscles to any number of triggers. See Box 10.3 for a list of possible triggers. Researchers are investigating the role of inheritance in asthma.

Method of Transmission: Not applicable

Epidemiology: Results of the 2009 National Health Information Survey (NHIS) show that approximately 39.9 million Americans have been diagnosed with asthma at some point in their lives (ALA, July 2011b). Asthma is the third leading cause of childhood hospitalizations (ALA, November 2011c). Women are afflicted with asthma more often than men, but only after puberty; until then, more boys than girls are affected. Asthma rates are significantly higher among blacks (43%) than whites (ALA, July 2011b).

Pathogenesis: The inflammatory response is elicited by exposure to one of the triggers. This causes mast cell degranulation (see Chapter 3) and the release of multiple chemical mediators, including histamine, prostaglandins, leukotrienes, and interleukins. The release of these substances causes smooth muscle spasm, mucosal edema, and the production of thick and tenacious mucus. The end result of this process is hyperresponsiveness or hyperexcitability of the airways and airway obstruction, which interferes with the release of air from areas of the lung distal to the obstruction and increases breathing difficulty. Individuals with asthma become cyanotic because they cannot exhale fully; therefore, they cannot inhale enough oxygen-rich air to keep the appropriate level of oxygen in the blood.

Extraoral Characteristics: After exposure to a trigger, the individual with asthma exhibits **paroxysms,** sharp spasms of wheezing, dyspnea, and cough. The wheezing initially appears during exhalation only but may affect inhalation as the attack progresses. Exhalation becomes so difficult the accessory muscles of expiration must be mobilized. Meanwhile, the individual becomes anxious adding to the hyperresponsiveness of the airways. Uncontrolled or prolonged attacks not relieved by the administration of medication are called status asthmaticus and are considered life-threatening emergencies.

Perioral and Intraoral Characteristics: Medications taken by individuals with asthma may contribute to several oral conditions. One of the most common oral side effects of

inhaled corticosteroids is an increased risk of oral fungal infections (candidiasis, Chapter 14). Many of the medications used to treat asthma have the potential to cause xerostomia (dry mouth), which is associated with a higher rate of caries and periodontal or gingival infections. In addition, an increase in gastroesophageal reflux, associated with some asthma medications, can cause a higher than normal oral pH (acidic), which is related to enamel erosion.

Distinguishing Characteristics: Inability to empty the lungs during an attack, causing decreased oxygen supply to the body

Significant Microscopic Features: Not applicable

Dental Implications: Dental hygienists have the opportunity to help individuals with asthma to maintain healthy oral tissues by educating them about the adverse effects of the drugs they may be taking such as an increased risk for caries or candidiasis. In addition, the dental hygienist should make home care recommendations focused on controlling the oral effects of the medications. A thorough review of the patient's medical/dental history should make the dental professional aware of the patient's risk for having an asthma attack during dental treatment. Steps should be taken to prevent exposing the patient to triggers and to facilitate treatment of the patient should an attack occur. Caution should be observed when recommending medications containing aspirin because aspirin-induced attacks may affect as many as one in five adults with asthma (Jenkins et al., 2004). Some preventive measures include stress management, aerosol control to limit the potential of inhaling foreign matter, and avoiding latex-containing gloves and disposables. The patient's medication should be available and readily accessible throughout the entire appointment. Patients should never be discharged from the dental office while still experiencing symptoms of an asthma attack, emergency medical services should be contacted, and treatment in a hospital emergency room is essential (Malamed, 2000).

Differential Diagnosis: Not applicable

Treatment and Prognosis: Medical therapy for asthma consists of the use of bronchodilators to open the airways and anti-inflammatory medications to interfere with and/or prevent the inflammatory response, such as leukotriene modifiers that block the action of leukotrienes (see Chapter 3) and corticosteroids. Emergency medical services should be summoned if the attack does not resolve after appropriate treatment has been given.

The most recent mortality data estimates 3,447 Americans died from asthma in 2007 (ALA, July 2011b).

NAME: Chronic obstructive pulmonary disease

Etiology: There are two forms of COPD: (1) emphysema and (2) chronic obstructive bronchitis. Smoking and inhaling secondhand smoke are the most common risk factors associated with COPD. In addition, air pollution, occupational exposure to toxic inhalants, heredity, and a history of childhood respiratory infections have been linked to cases of COPD (ALA, February 2011a).

Method of Transmission: Not applicable

Epidemiology: In 2008, an estimated 13.1 million Americans had COPD, most having chronic obstructive bronchitis. Most of those affected were over the age of 45, and most were whites. In recent years, males and females have been equally affected (ALA, February 2011a). However, 2007 marked the eighth year in a row women outnumbered men in the number of deaths attributed to COPD (ALA, February 2011a).

Pathogenesis: Emphysema is characterized by decreased elasticity of lung tissue and destruction of alveolar tissue, resulting in enlarged air spaces and increased total lung capacity. Chronic obstructive bronchitis is characterized by obstruction of the small airways by inflamed, hyperplastic mucosal tissues accompanied by excessive production of mucus.

Extraoral Characteristics: Individuals with emphysema have been called "pink puffers" because they are able to maintain normal blood oxygen levels by increasing their rate of breathing. They often present with an increase in the size of the chest or "barrel chest" because of air becoming trapped in the lungs. Exhaustion after minor activity is common due to the amount of energy required to just keep breathing. Eating becomes a problem because the individual cannot stop breathing long enough to swallow, and drastic weight loss is often experienced in advanced disease due to increased caloric needs from the exertion required to breathe and decreased caloric intake.

Individuals with chronic obstructive bronchitis have been called "blue bloaters" because they cannot maintain a normal level of oxygen in their blood by simply increasing their respiratory rate. Cyanosis is common in chronic bronchitis and occurs because the airways are blocked by inflamed and hyperplastic tissues and by excessive mucus and fluids that interfere with oxygen exchange. These individuals have marked shortness of breath and usually present with a productive cough that has worsened over the course of many years.

Perioral and Intraoral Characteristics: Not applicable

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: Maintaining patient comfort and an adequate oxygen level during dental treatment is imperative. The position of the dental chair may have to be modified so the patient is able to breathe comfortably and supplemental oxygen may be indicated. Procedures that create aerosols, such as ultrasonic scaling and air abrasion or polishing, should be avoided in most cases. Tobacco cessation interventions are appropriate for patients who continue to smoke but want to quit.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Most patients seek medical care when COPD is in an advanced stage. The lung damage is irreversible, but treatments are available that can improve the individual's quality of life. Common medications used to control symptoms and slow progression of the disease include (1) bronchodilators that open the airways, (2) anti-inflammatory medications that inhibit or prevent the inflammatory response, and (3) expectorants that help to clear excess mucus from the lungs. By far, the most important adjunct to treatment is tobacco cessation for those who smoke. In 2007, 124,777 Americans died from COPD. Eighty-five to ninety percent of these deaths were caused by smoking (ALA, February 2011a).

NAME: Cystic fibrosis

Etiology: CF is an inherited disorder resulting from a mutation of the *CFTR* gene on chromosome 7.

Method of Transmission: CF follows an autosomal recessive inheritance pattern.

Epidemiology: According to the American Lung Association, 30,000 Americans have CF, and 1,000 new cases are diagnosed each year. It affects predominately white populations, with equal distribution among males and females and is considered the second most common inherited disorder (sickle cell anemia is first) of childhood in the US population (ALA, 2010).

Pathogenesis: The genetic abnormality causes the development of defective epithelial cells that (1) line the bile, pancreatic, and sweat ducts and (2) line the respiratory system. The defective cells produce abnormally thick mucus that obstructs the lumina of the affected organs. Blocked pancreatic ducts decrease fat metabolism and decrease the absorption of fat-soluble vitamins such as A and K resulting in malnourishment and low body weight. Excessive salt is lost through defective sweat glands causing electrolyte imbalance and leaving the individual susceptible to heat exhaustion. The most serious complications involve the lungs, resulting in chronic pulmonary disease, frequent infection, and eventual scarring of the lung tissue. Death is usually the result of respiratory failure related to the damage done by repeated lung infections.

Extraoral Characteristics: The most common symptoms of CF are chronic coughing or wheezing accompanied by recurrent severe lung infections. The individual with CF may be underweight and may have a barrel chest. One of the characteristic findings is clubbing of the fingers due to hypoxia (Fig. 10.3). Osteoporosis and diabetes are considered common sequela of this disease as well.

Perioral and Intraoral Characteristics: Salivary glands, especially those glands producing mucous secretions, are often affected by CF leading to decreased flow and altered composition of saliva. Medications may also increase xerostomia and/or change the quality of the saliva. These patients usually present with a high caries risk, which is then exacerbated by the frequent ingestion of high-caloric foods necessary to maintain an appropriate weight. They also have an increased risk for oral fungal infections because inhaled corticosteroids are often used to control asthma-type attacks.

Inadequate levels of vitamin K may cause excessive gingival bleeding, especially in the presence of oral infections.

FIGURE 10.3. Cystic fibrosis. Clubbing of the fingertips is considered a classic but uncommon sign of CF. ("Clubbing CF," © Jerry Nick, MD, used under a Creative Commons Attribution 3.0 Unported: *http://creativecommons.org/licenses/by/3.0/*)

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: Patients with CF may take prophylactic antibiotic medications to prevent lung infections (usually from *Staphylococcus aureus* or *Pseudomonas aeruginosa*) for their entire lives. Medical consultation should be obtained to determine any need for additional prophylactic antibiotics to decrease the risk of respiratory infection due to aspiration of oral bacteria aerosolized during dental procedures. Exposure to aerosols should be minimized with high-volume evacuation and preprocedural rinses. Patient positioning should optimize respiration and aid in mucus drainage. Patients with CF are not considered candidates for nitrous oxide analgesia because the gas may cause the cystic spaces in the lungs to expand (Clark, 2009). Vitamin K supplements may be needed to enhance blood clot formation prior to procedures in which bleeding is anticipated. Home care recommendations should focus on preventing caries and maintaining healthy oral tissues, which will in turn decrease the number of oral bacteria (DeAngelis, 2001).

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment focuses on preventing complications associated with CF. Inhaled and oral

antibiotics are used to treat and prevent lung infections. Other inhaled drugs are used to thin out the thick mucus in the lungs. Bronchodilators help open airways, and mechanical chest therapy helps to break up mucus in the lungs. Vitamin supplements, pancreatic enzyme supplements, oral corticosteroids, anti–gastroesophageal reflux medications, and laxatives are frequently used to manage the effects of the disease. Lung transplantation is being offered to those with advanced lung damage, but transplants will not cure the disease, only extend the life of the individual for a short time. Research focusing on gene therapy is showing some promise.

The prognosis for those affected by this disease is improving. The predicted median survival age for someone with CF is 35-39 (CFF, 2012).

Gastrointestinal System Disorders

The GI system is responsible for the ingestion, digestion, and absorption of food, as well as the elimination of wastes from the body. The oral cavity is the starting point for the actions of this system. Mastication (chewing) breaks the food into small pieces and mixes it with saliva. Saliva lubricates the bolus of food and contains salivary amylase, which starts the digestion of carbohydrates. The food is swallowed in a complex action that is usually automatic. The motor impulses for swallowing are supplied by the trigeminal, glossopharyngeal, vagus, and hypoglossal cranial nerves. Once the bolus is moved into the esophagus and swallowed, involuntary muscle contractions cause **peristalsis** (rhythmic muscle contractions that propel food toward the stomach). The lower esophageal sphincter controls the entrance of food into the stomach and is the culprit when food and gastric juices back up out of the stomach and into the esophagus during vomiting and in cases of gastric reflux. The stomach is lined by special mucosal cells that secrete both digestive enzymes and the hydrochloric acid, which activates the enzymes. The surface of the stomach is protected from the acidic environment by copious amounts of thick mucus also secreted by cells within the mucosal lining. Gastric juices mix with the food and create a semidigested mixture called chyme, which is released from the stomach through the pyloric sphincter into the small intestine, where peristalsis moves it along. Most of the digestion of food takes place in the upper part of the small intestine, or duodenum. Here, the pancreas secretes enzymes through the pancreatic duct, which aid in the digestion of proteins, lipids, and carbohydrates. It also secretes an alkaline substance that neutralizes the acid from the stomach. Bile, manufactured in the liver, enters the duodenum from its storage area in the gall bladder through the common bile duct. Bile is an **emulsifier** (a substance that allows fat to mix with water) that facilitates the digestion of lipids. The nutrients are absorbed into capillaries and lymph vessels found in the surface of the small intestine, which is covered with many tiny projections called villi. The villi tremendously increase the available surface area, thereby helping to absorb as many nutrients as possible. The remaining substance passes through the small intestine into the large intestine, where water and minerals are absorbed into the body. The remaining waste is eliminated as feces. Many GI disorders have oral manifestations associated with them. This section discusses a few of the more common disorders.

NAME: Dysphagia

Etiology: Dysphagia, difficulty swallowing, can result from a physical obstruction or a muscular or neurologic disorder. Tumors (neoplastic growths) and pockets (**diverticula**) that form in the wall of the esophagus can obstruct the flow of food from the mouth to the stomach. Individuals with scleroderma (see Chapter 23) may exhibit fibrosis of the muscle layer in the esophagus, causing dysphagia. Poststroke dysphagia affects between 51 and 73% of persons with a history of stroke. Strokes cause damage to nerves controlling the muscles of swallowing impairing a person's ability to safely swallow food. In addition, the normal aging process alters tongue and swallowing function to some extent making dysphagia more common in older adults.

Method of Transmission: Not applicable

Epidemiology: Not applicable

Pathogenesis: The development and progression of this condition vary depending on the etiology.

Extraoral Characteristics: Swallowing difficulties associated with nerve or muscle dysfunction can cause food to be aspirated into the lungs, resulting in pneumonia. This type of dysphagia can also cause the regurgitation of food and can limit the individual's ability to ingest adequate nutrients, resulting in malnourishment.

Perioral and Intraoral Characteristics: Pain occurring during and within 2 to 5 seconds after swallowing usually indicates a problem in the upper esophagus, while pain occurring 10 to 15 seconds later indicates a lower esophageal problem. If the dysphagia is due to diverticula, food may lodge in the pouches and ferment, causing a foul odor and increasing the risk of infections.

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: The patient must be properly positioned in the dental chair to decrease the risk of accidental aspiration of oral fluids during dental treatment. Dietary modifications necessary for decreasing problems associated with dysphagia may encourage increased caries activity, and preventive strategies should be included in home care recommendations.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment depends on the cause of the dysphagia. Physical therapy to train muscles that control mastication and swallowing has helped in cases

of stroke or other neurologic impairments. Eating small meals, eating slowly, and preparing foods in an easier-to-swallow form, such as thickening liquids, are important elements for managing dysphagia. The main objectives of treatment are maintaining proper nutrition and hydration, eliminating pain, and preventing aspiration of food into the lungs.

NAME: Gastroesophageal reflux disease

Etiology: Gastroesophageal reflux disease (GERD) is caused by a weak lower esophageal sphincter that allows the flow of gastric contents back into the esophagus.

Method of Transmission: Not applicable

Epidemiology: Twenty-five to forty percent of the US population experiences symptoms of GERD at some point in their lives, while approximately 7 to 10% suffer from GERD every day. Males and females are equally affected, and while the disorder can occur at any age, it occurs more frequently over the age of 40 (Patti et al., 2011). Barrett esophagitis occurs in about 376 of every 100,000 men and women in the United States. (Johnston & Eastone, 2011).

Pathogenesis: Exposure of the esophagus to gastric acid causes mucosal erosions that can eventually cause permanent tissue damage. The most severe form of damage is called Barrett esophagus and is associated with an increased risk of esophageal adenocarcinoma.

Extraoral Characteristics: The most common symptom is heartburn that occurs 30 to 60 minutes after eating, gets worse if the person lies down or bends over, and is relieved somewhat by being in the upright position. Belching, wheezing, chronic cough, and hoarseness are common symptoms as well as varying degrees of pain located in the chest, throat, shoulder, or back. Often, the pain is so intense it is confused with angina or myocardial infarction and emergency medical care must be obtained to determine the exact cause.

Perioral and Intraoral Characteristics: GERD is associated with an increased risk of enamel erosion in some individuals (Fig. 10.4). GERD may be associated with a higher-than-normal risk of pharyngeal cancer (El-Serag et al., 2001).

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: Dental appointment modifications include positioning the patient chair in a more semiupright position for the patient comfort, especially during longer appointments. Specific attention should be given to the pharyngeal area during the intraoral examination, because of the potential for an increased risk of cancer associated with GERD. Education about the oral effects of GERD and recommendation of additional fluoride to counteract increased levels of oral acid are appropriate. Custom trays can be fabricated to provide optimal contact between the teeth and the fluoride and fluoride varnish can be applied on a 3-month schedule. The patient should be warned about the potential for exacerbating the loss of tooth structure by toothbrushing and bruxism. Recommendations may include determining when brushing would be least likely to cause damage and using a mouth guard for double duty, to hold fluoride and prevent attrition, during sleep.

FIGURE 10.4. Enamel erosion. This extensive enamel erosion was seen in an individual with chronic severe GERD of more than 10 years' duration.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment includes using medications to decrease the production of acid in the stomach, modifying eating habits, and avoiding foods that cause the lower sphincter to be less effective, such as alcohol, caffeine, chocolate, and fats. Smoking has been associated with an increased risk of GERD; therefore, cessation therapy is advised for those suffering from this disorder. Reflux occurs more easily when the person is in a supine position, and sleeping with the head elevated is advised. Managing the oral effects of GERD may involve restoring the teeth affected by erosion using crowns or other appropriate restorative techniques and constructing a mouth guard or fluoride tray to help prevent further damage.

NAME: Peptic ulcer

Etiology: Peptic ulcers occur in the duodenum and less frequently in the stomach. The most common cause of peptic ulcer is infection with *Helicobacter pylori* (*H. pylori*); the second most common cause is medications containing aspirin or other nonsteroidal anti-inflammatory drugs (NSAIDs). Other factors associated with peptic ulcers include older age, prior history of peptic ulcer, the concurrent use of warfarin, and the use of corticosteroid drugs (Porth, 2011).

Method of Transmission: Not applicable

Epidemiology: About 6.4% of the US population self-reported peptic ulcer during 2010 (Vital and Health Statistics, 2012).

Pathogenesis: Infection with *H. pylori* causes gastric mucosa inflammation, which weakens the mucosal surface

increasing its susceptibility to injury; likewise, NSAIDs interfere with the production of mucus. Both processes compromise the effectiveness of the mucosal barrier in the stomach or small intestine. Once the barrier is compromised, underlying tissues come in contact with the acidic gastric contents, and ulceration occurs. If left untreated, the ulcers can cause excessive loss of blood, perforation of the stomach or duodenum, obstructions due to swelling associated with inflammation, or scarring associated with repeated injuries.

Extraoral Characteristics: Pain relieved by eating is the most common presentation of peptic ulcers. Anorexia, weight loss, and vomiting are more common with ulcers in the stomach than those in the duodenum. Approximately 20% will have bleeding or hemorrhage, and about 5% will develop a perforation of the stomach or duodenum.

Perioral and Intraoral Characteristics: Enamel erosion may be present.

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: Frequent eating to alleviate pain may increase caries activity, especially if cariogenic foods are chosen. Vomiting, if present, increases the risk of enamel erosion, and the patient should be advised about not brushing immediately after vomiting. Home fluoride treatments and nutrition counseling should be considered for these patients.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment focuses on eliminating the infection and decreasing the acid level in the stomach. The most common therapy is a combination of antibiotics with drugs that lower the amount of acid produced (such as proton pump inhibitors). When aspirin and/or NSAIDs are the cause of the ulcers, the most appropriate course of action is to eliminate the drugs. This may not always be possible; therefore, the use of antacids and drugs to lower the acid levels may be helpful. The prognosis for most patients is excellent.

NAME: Crohn disease

Etiology: Crohn disease is most likely a multifactorial disease associated with a strong genetic predisposition and environmental and host factors.

Method of Transmission: Studies show evidence of a genetic predisposition; otherwise, Crohn disease is not transmissible.

Epidemiology: Crohn disease occurs in about 7 per 100,000 individuals in the United States. Most are diagnosed before the age of 30 and women are affected slightly more often than men (Rangasamy et al., 2011).

Pathogenesis: Crohn disease is a chronic inflammatory disorder of the granulomatous type that affects the GI tract anywhere from the oral cavity to the anus. The characteristic ulcerative lesion involves all layers of the tissues in the GI tract and may be found scattered among normal mucosal tissues. The ulcerations usually progress into deep fissures, which may form fistulas that communicate with other parts of the GI tract or with the skin, bladder, or vagina. Fistulas have the potential to become infected, thereby creating abscesses. The chronic nature of the inflammation causes affected tissues to become fibrotic and thickened, leading to malabsorption syndromes. The risk of colon cancer is increased in those with long-term disease (Rangasamy et al., 2011).

Extraoral Characteristics: The most common symptom is prolonged diarrhea with abdominal pain. Vitamin deficiencies associated with malabsorption of nutrients are common, as are weight loss, low energy levels, and low-grade fevers. Children with Crohn disease are likely to experience growth retardation. Ulcers that perforate the mucosal lining of the GI tract may cause chronic loss of blood, resulting in anemia.

Perioral and Intraoral Characteristics: Compromised mucosal tissues result in multiple, large, aphthous-like ulcers on the buccal and labial mucosa and the tongue, and because the lower layers of the mucosa are affected, they are usually deep. Other oral manifestations may include diffuse swelling of the buccal and labial mucosa, angular cheilitis, glossitis, and cobblestoning (mild fissuring) of the buccal mucosa. The oral manifestations are usually associated with exacerbation of the intestinal symptoms and tend to resolve when the intestinal disease is under control (Gurenlian, 2003).

Distinguishing Characteristics: Cobblestoning of the buccal mucosa might be considered a distinguishing feature.

Significant Microscopic Features: Not applicable

Dental Implications: The patient should be educated about the benefits of maintaining a healthy oral environment as a means of helping to prevent the oral complications of Crohn disease. Pain management should be accomplished without using NSAIDs or aspirin-containing products, since they tend to affect the mucosal tissues of the GI tract.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment focuses on controlling the inflammation, eliminating or preventing nutritional deficiencies, preventing complications, and relieving symptoms. Current therapies include medications such as anti-inflammatories, immunosuppressants, antidiarrheal agents or laxatives, and some new drugs that affect certain chemical mediators crucial to the activation of the inflammatory response (tumor necrosis factor [TNF]). Nutritional supplements are necessary to prevent nutrient deficiencies. If these treatments are unsuccessful or if there are complications such as fistula or abscess formation, surgery to remove the diseased section of the intestine

is indicated. Occasionally, patients must have their entire colon removed, after which solid wastes are removed through a colostomy and collected in a colostomy bag. Oral lesions are treated with topical steroids, if necessary.

Crohn disease is a chronic debilitating disease characterized by frequent remissions and exacerbations. A slightly higher risk for GI cancer is associated with a minimal increase in mortality rates for those with Crohn disease (Rangasamy et al., 2011).

NAME: Peutz-Jeghers syndrome

Etiology: Peutz-Jeghers syndrome is an inherited condition that results from a mutation of the *serine/threonine protein kinase* (*STK11*)*/liver kinase B1*(*LKB1*) tumor suppressor gene on the short arm (p) of chromosome 19.

Method of Transmission: Peutz-Jeghers syndrome follows an autosomal dominant inheritance pattern or occurs as a spontaneous mutation.

Epidemiology: Peutz-Jeghers is rare in the United States occurring in about 1 case in 60,000 to 300,000 people.

Pathogenesis: The genetic defect causes inactivation of a gene that produces a protein called kinase. This leads to an increased risk for cancers in the breast, lung, pancreas, gonads, and thyroid (Rubin et al., 2012).

Extraoral Characteristics: Brown or dark blue flat mucocutaneous pigmentations are present in at least 95% of cases; extraorally, they form on the skin of the face, hands and fingers, and feet and toes. Individuals with this genetic mutation have multiple intestinal polyps that resemble neoplastic growths but are comprised of normal cells and grow at a normal rate. The polyps may also occur in the stomach or the colon. This genetic disorder is associated with a significantly increased risk for developing cancers of the breast, pancreas, testis, and ovary in addition to the increased risk of developing adenocarcinoma of the lining of the GI tract.

Perioral and Intraoral Characteristics: Perioral and intraoral brown or dark blue macules form on and around the lips and vermilion border, perinasal skin, and buccal mucosa (Fig. 10.5).

Distinguishing Characteristics: The striking melanin pigmentations are characteristic of this condition.

Significant Microscopic Features: Not applicable

Dental Implications: Dental professionals should be aware of the characteristic pigmentation associated with Peutz-Jeghers and make appropriate referrals when indicated because of the significantly elevated risk of developing cancers.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment consists of identification of the syndrome and careful monitoring of the tissues at risk for cancer development. Intestinal polyps are usually removed when discovered during colonoscopy. Approximately 3% of patients develop intestinal adenocarcinoma (Rubin et al., 2012).

Malabsorption Syndromes

Malabsorption refers to the body's inability to absorb specific substances from the digestive tract. The substances can be vitamins, minerals, or fats. There are several causes associated with malabsorption syndromes, including chronic intestinal disease, removal of large sections of the intestine, deficiency of specific digestive enzymes, or

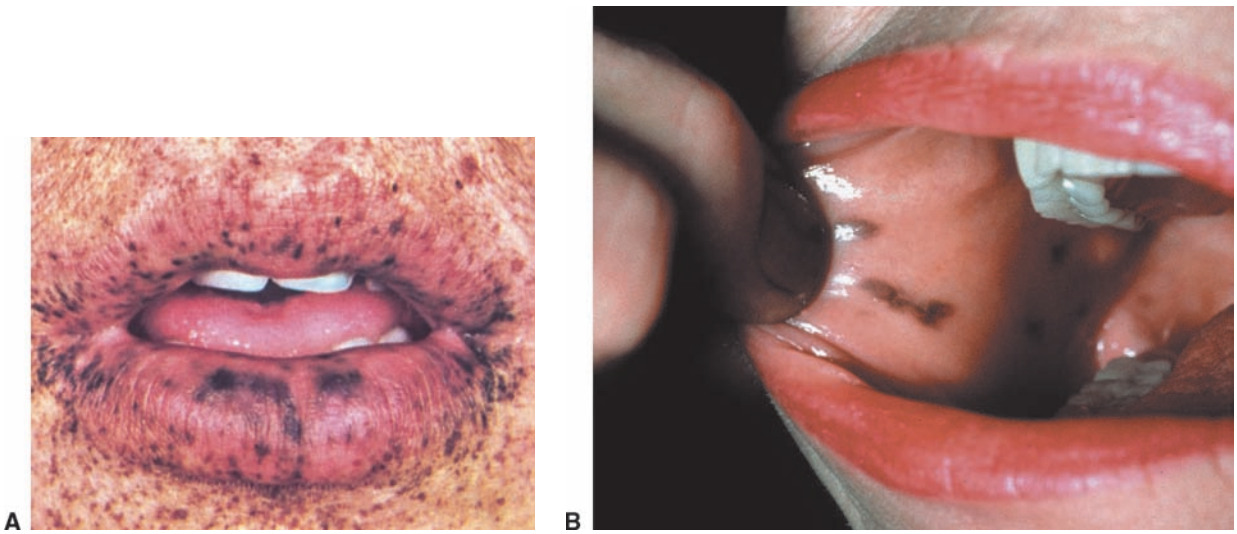

FIGURE 10.5. Peutz-Jeghers syndrome. **A.** This syndrome presents with pigmented spots on the lips that are more prominent than the freckling of the surrounding skin. The hands and face may also have scattered pigmented spots. (From Robinson HBG, Miller AS. Colby, Kerr, and Robinson's color atlas of oral pathology. Philadelphia: JB Lippincott, 1990.). **B.** Pigment in the buccal mucosa helps to confirm the diagnosis. (From Mulholland MW, Maier RV, et al. Greenfield's surgery scientific principles and practice. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2006.)

deficiency of bile acids. A common example of a malabsorption syndrome is lactose intolerance, which is caused by a lactase deficiency, or the production of a defective lactase enzyme. Lactose intolerance leads to the accumulation of undigested lactose in the intestine. Bacteria ferment the lactose, producing gases that cause pain, bloating, and flatulence. Diarrhea is a common symptom due to a change in the rate of water absorption caused by the abundance of lactose. Once a malabsorption syndrome has been identified, most can be controlled by avoiding foods that exacerbate the condition, providing supplements to prevent nutrient deficiencies, and in some cases replacing deficient enzymes. Celiac disease is an example of a malabsorption syndrome associated with some specific oral manifestations.

NAME: Celiac Disease (celiac sprue, glutton-sensitive enteropathy)

Etiology: Celiac disease is a complex genetic disorder associated with multiple genes (Wolters & Wijmenga, 2008). The symptoms of celiac disease are caused by an immune response to gluten found in wheat, rye, barley, and triticale.

Method of Transmission: Celiac disease has a strong hereditary component, but otherwise, it is not transmitted.

Epidemiology: Population-based studies estimate this condition affects approximately 3 million people in the United States or about 1% of the population (Klapproth & Yang, 2011). It is estimated that about 90% of these people are not aware they have the condition (Rashid et al., 2011).

Pathogenesis: Gluten appears to trigger an autoimmune reaction in which the intestinal villi are destroyed, leaving large ulcerative lesions resulting in poor nutrient absorption across the affected mucosal surfaces (Porth, 2011).

Extraoral Characteristics: Diarrhea, fatty stools, flatulence (passing gas), bloating, pain, and cramping are all associated with ineffective absorption of fats. Anemia is associated with decreased absorption of iron and folic acid. Other symptoms are related to deficiencies of vitamins A, D, E, and K. Vitamin K is essential for proper clot formation, and any deficiency is associated with increased bleeding. Deficiencies of calcium and vitamin D are associated with osteopenia and osteoporosis. Patients may exhibit varying amounts of weight loss, weakness and fatigue, and failure to thrive or growth retardation in children. Dermatitis herpetiformis, a pruritic, vesicular skin rash, affecting the skin of the trunk, buttocks, neck, and scalp and overlaying the joints of the extremities is seen in about 10 to 20% of those with celiac disease (Fig. 10.6).

Perioral and Intraoral Characteristics: Malabsorption syndromes like celiac disease are associated with oral ulcers, glossitis (Fig. 10.7), and angular cheilitis, all of which are linked to nutrient deficiencies. Celiac disease is also associated with varying degrees of enamel defects such as scattered white spots, linear discolorations, and rough, grooved or pitted surfaces (Rashid et al., 2011). Patients with celiac disease have an increased risk of lymphoma and cancer of the oropharynx, esophagus, and pancreas.

FIGURE 10.6. Dermatitis herpetiformis. One of the cutaneous findings associated with celiac disease. (Courtesy of W. Witmer; Elder AD, Elenitsas R, Johnson BL, et al. Synopsis and atlas of lever's histopathology of the skin. Lippincott Williams & Wilkins, Philadelphia, 1999, p 2, clin. fig. IA1; p 163&#0.)

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: Dental hygienists and dentists should identify individuals who present with enamel defects and a history of recurrent oral ulcers and question them about other symptoms they may have such as weight loss, diarrhea, abdominal pain, anemia, and extreme fatigue that are associated with celiac disease. If this is suspected, the patient should be referred to a physician for a medical evaluation.

FIGURE 10.7. Glossitis due to a malabsorption syndrome. Vitamin or iron deficiencies that result from malabsorption syndromes cause atrophy of the papillae and create a smooth, often sore, tongue. (From Weber J, Kelley J. Health assessment in nursing. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

Differential Diagnosis: Not applicable

Treatment and Prognosis: The treatment is total elimination of gluten from the diet. Corticosteroids may be necessary for some who do not respond to diet alone. Normally, the prognosis is excellent, but for those who do not respond to diet or treatment or are not compliant, the prognosis is considered poor (Klapproth & Yang, 2011).

Nervous System Disorders

The nervous system is designed to receive sensory information, process it, and determine what actions to take to maintain homeostasis. It also protects the body with little or no conscious thought by the individual. There are two main parts of the nervous system: (1) the central nervous system (CNS), which consists of the brain and the spinal cord, and (2) the peripheral nervous system (PNS), which consists of all nervous tissues found outside of the CNS. The neuron is the basic cell of both systems. The neuron is so specialized that other cells must help to provide nutritional and other metabolic support. Schwann cells provide nutritional and metabolic support for the PNS; glial cells, such as the oligodendroglia, provide these functions for the CNS. These cells also produce the myelin sheaths covering the axons of the neurons. Myelin increases the rate of transmission of a nerve impulse and is necessary for the continued existence of the axon.

The nervous system requires a continuous source of glucose and oxygen in order to remain functional, and since the cells are unable to store these elements, they rely on the circulating blood to provide them. In addition, unlike some other tissues, nervous tissue cannot undergo anaerobic metabolism. Nerve cells become nonfunctional after about 10 seconds without oxygen and begin to die within 4 to 6 minutes. The disorders discussed in this section have their basis in the tissues of the nervous system.

NAME: Meningitis and encephalitis

Etiology: Meningitis is an inflammation of the meninges, the membranes that cover the brain and the spinal cord. Encephalitis is an inflammation of the nerve tissues of the brain and/or spinal cord. Both of these conditions can be caused by a variety of organisms. Bacteria such as *Streptococcus pneumoniae* and *Neisseria meningitidis* (meningococcal meningitis) are the most common cause of bacterial meningitis. Viral meningitis is most often associated with enteroviruses, such as coxsackievirus B; however, mumps, Epstein-Barr, and herpes simplex viruses have all been linked to the infection. Encephalitis can be caused by bacteria, viruses, fungi, or other organisms. Rabies is an example of a virus that specifically targets the nervous tissue of the brain, causing encephalitis. Herpes simplex is one of the more common agents associated with viral encephalitis. Viruses carried by insects such as mosquitoes and ticks may also cause encephalitis. Western and Eastern equine encephalitis are carried by mosquitoes from infected animals to the humans they bite next.

Method of transmission: Both encephalitis and meningitis are transmitted through similar routes. The pathogenic organisms gain entry by way of traumatic injury, ear infections, and infectious organisms from distant sites in the blood circulating through the area, such as a meningococcal bacteremia and more.

Epidemiology: Approximately 0.6 to 4 individuals per 100,000 population contract meningococcal disease in the United States every year (Razonable et al., 2011). Of interest is the fact college students who reside in dormitories are 9 to 23 times more likely to contract this infection than students who live off campus (CDC, 2005).

Pathogenesis: In meningitis, the organisms infect all layers of the covering of the brain and/or the spinal cord. Bacterial infection produces purulent exudate that blocks movement of the cerebrospinal fluid and pinches off the capillary blood supply, causing tiny infarcts in the tissues. If not treated, the infection causes edema of the brain, coma, and death. Viral meningitis follows a less severe, self-limiting course, with no production of purulent exudate.

Encephalitis causes generalized edema, hemorrhage, and necrosis of brain and spinal tissues. Most forms of encephalitis target specific areas of the CNS.

Extraoral Characteristics: Meningitis and encephalitis exhibit similar symptoms of headache, stiff neck, fever, chills, nausea, vomiting, altered mental status, and pain in the back, abdomen, and extremities. Meningitis symptoms often have an abrupt onset with rapid development of symptoms, sometimes leading to death within 24 hours. Individuals with meningitis may exhibit a petechial rash covering large portions of the body.

Perioral and Intraoral Characteristics: Not applicable

Distinguishing Characteristics: The rapid onset of headache and stiff neck are characteristic symptoms of these infections.

Significant Microscopic Features: Not applicable

Dental Implications: Dental professionals need to be aware of the signs and symptoms of these infections to make an appropriate medical referral if they are observed in a patient.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment depends on the etiologic agent. Antibiotics are given for a bacterial infection. Corticosteroids are often given to offset the inflammatory response to massive bacterial deaths and the subsequent release of endotoxins from the cell walls.

The CDC recommends routine immunization against *N. meningitidis,* the most common cause of bacterial meningitis, for all preadolescents, teenagers, and college-bound students (CDC, 2005).

The prognosis depends on the general health and immune status of the individual. The highest mortality rates

are associated with individuals who have a compromised immune system, low level of consciousness, and infection with *S. pneumoniae*. In any case, the potential exists for neurologic damage causing seizures and decreased mental capacity after resolution of the infection.

NAME: Parkinson disease

Etiology: Parkinson disease (PD) is a degenerative disease of the basal ganglia located at the base of the cerebral hemisphere. The exact cause is unknown; however, genetic, viral, and environmental agents have been suggested. Genetic factors may be more involved with PD that occurs early in life, at about 40 years of age.

Method of transmission: Approximately 10% of PD cases have genetic-based etiologies; otherwise, PD is not transmissible.

Epidemiology: The Parkinson's Disease Foundation estimates over 1 million Americans are affected by PD, with 60,000 new cases diagnosed annually. The disease occurs more often in men and more frequently in those over the age of 50 (PDF, no date).

Pathogenesis: PD originates within a region in the brainstem called the substantia nigra. Cells within the substantia nigra produce the neurotransmitter dopamine, which enables cells of the CNS to function correctly, thereby controlling movement and balance. In PD, the cells of the substantia nigra are destroyed, and the level of dopamine decreases, causing a syndrome of abnormal movement. This syndrome is characterized by **bradykinesia** (slowed movements), resting tremor (alleviated by voluntary movement), muscle rigidity, and postural abnormalities.

Extraoral Characteristics: See Figure 10.8 for a listing of the physical characteristics of PD. Nonmotor symptoms are associated with autonomic nervous system dysfunction and can include sleep disturbances, depression, dementia, constipation, hyperhidrosis (excessive sweating), and urinary incontinence.

Perioral and Intraoral Characteristics: Patients with PD often exhibit masklike facial features. Tremors affect the muscles of mastication and facial expression. Constant **parafunctional** (not related to mastication) jaw movements cause an increase in enamel attrition and **abfraction** (loss of tooth structure due to biomechanical forces). As the disease progresses, muscles of the tongue and throat become more rigid resulting in dysphagia and unintelligible speech. Dysphagia may become so severe the patient is unable to eat and must be fed through a feeding tube. Drooling occurs because of infrequent swallowing and pooling of the saliva in the anterior of the mouth.

Distinguishing Characteristics: Slowed movements, resting tremor, muscle rigidity, and postural abnormalities are characteristic of this condition during early stages.

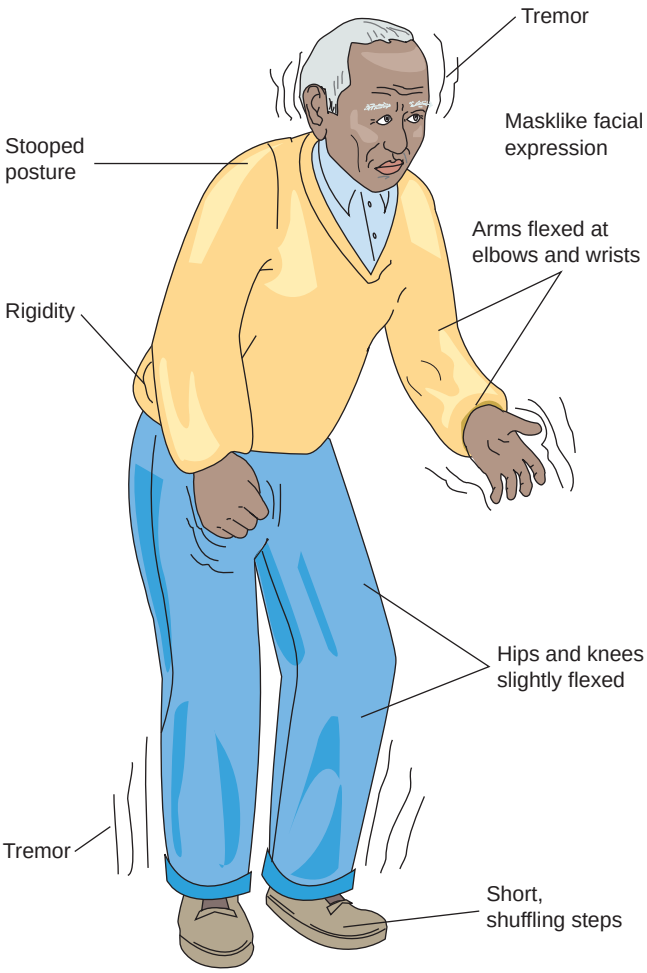

FIGURE 10.8. Parkinson disease. Illustration showing the typical physical characteristics of Parkinson disease. (Timby BK, Smith NE. Introductory medical–surgical nursing. 8th ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

Significant Microscopic Features: Degeneration of the neurons in the substantia nigra

Dental Implications: Dental health care workers need to modify some of their appointment procedures for patients who have PD. All precautions should be taken to avoid patient and operator injuries from sharp instruments that may occur due to the uncontrolled motions characteristic of this disease. Mouth props and bite blocks may help to keep the mouth open and stable. Also, the use of a rubber dam may avoid saliva contamination during restorative procedures. Pillows or gentle hand pressure will help to stabilize the patient's head in the headrest during treatment. The patient should be gradually raised from the supine position after dental care, since some medications given to control PD may cause postural hypotension. Xerostomia is a side effect of many of the PD medications, and frequent use of fluoride is recommended. It is difficult for some patients with PD to tolerate the normal tray delivery; therefore, fluoride varnish instead of trays is recommended. Supplemental fluoride in the form of a gel,

not rinse, should be used daily. Frequent short appointments instead of fewer long appointments work better for these individuals and early morning is the best time of day for many. The Parkinson's Disease Foundation suggests patients take levodopa 60 to 90 minutes prior to the dental visit to take advantage of the peak response period (PDF, no date). Regular maintenance appointments to monitor oral health are very important and should be scheduled as often as necessary to maintain oral health. Every effort should be made to adapt home care implements to the specific needs and abilities of the patient, to provide independence for as long as possible. Examples of modifications include increasing the width of toothbrush handles and using floss holders. The mechanical toothbrush is recommended for most patients because it performs most of the work with little effort on the part of the patient and it is easier for caregivers to use. Caregivers should be trained to use appropriate home care procedures to maintain the patient's oral health when necessary (Mitchell, 2006).

Differential Diagnosis: Not applicable

Treatment and Prognosis: Medical treatment is available for the symptoms of PD, but no treatment will reverse the course of the disease. Drugs that prevent the degradation of dopamine and thereby increase its availability are currently in use. Other drugs stimulate the same receptors as dopamine on the neurons, mimicking its action and decreasing the need for dopamine. All patients with PD will eventually take levodopa, a drug that is converted to dopamine by the body, thereby elevating its level. Long-term therapy with levodopa and continued neural degeneration often produces **dyskinesias** that present as uncontrollable movements including writhing, twitching, and shaking. Continued use of levodopa at this time is usually not tolerated by the patient, and other means of controlling symptoms should be considered. Surgery is one of these options. Irreversible surgical procedures destroy specific portions of the brain involved with the creation of movements, while sparing sensory and motor neurons. Deep brain stimulation is a safe and effective treatment that uses implanted electrodes to produce constant electrical stimulation of areas of the brain that affect unwanted motions. This procedure provides dramatic improvement in symptoms for many people for 5 years or longer, but it does not stop the progression of the disease (PDF, no date).

Continued neural degeneration eventually leads to death, often from aspiration pneumonia. PD is considered the 14th leading cause of death in the United States, with 7.1% of the total deaths (21,963) being attributed to it in 2010 (Murphy et al., 2012).

NAME: Bell palsy (facial nerve paralysis)

Etiology: The prime suspects in most cases of Bell palsy are infectious agents including herpes simplex (NINDS, 2011). Box 10.4 lists examples of suspected etiologic agents associated with Bell palsy.

BOX 10.4 Suspected Etiologies Associated with Bell Palsy

- Birth trauma
- Accidental trauma
  - Brain injuries
  - Facial injuries
  - Electrical injuries
- Infections
  - Herpes simplex and numerous other bacterial and viral organisms
  - Ramsey-Hunt syndrome
  - Otitis media
- Diabetes
- Hyperthyroidism
- Hypertension
- Pregnancy
- Neoplastic growths
- Alcoholism
- Iatrogenic
  - Mandibular block injections
  - Postimmunization
  - Parotid or mastoid surgery
  - Tonsillectomy
  - Dental surgery
- Idiopathic
  - Familial
  - Melkersson-Rosenthal syndrome
  - Multiple sclerosis
  - Myasthenia gravis
  - Sarcoidosis

Method of transmission: Other than transmission through infectious agents associated with Bell palsy, this disorder is not transmissible.

Epidemiology: Bell palsy affects approximately 40,000 individuals in the United States per year. Males and females are affected equally, and most have unilateral paralysis of the right side. Those under the age of 15 and over the age of 60 are affected less often than those between the ages of 15 and 60. Individuals with diabetes, pregnant women, and those with upper respiratory infections have the highest risk of developing this condition (NINDS, August 2011; Taylor et al., 2011).

Pathogenesis: The specific pathogenesis depends on the etiology of the paralysis. The paralysis is thought to result from edema and compression of the nerve, or **demyelination** (loss of the myelin sheath), and subsequent death of the neurons. The end result, however, is total or partial paralysis of the tissues innervated by the affected facial nerve (Fig. 10.9). The severity of the dysfunction is rated on a scale from mild dysfunction to total paralysis. The functions evaluated include forehead wrinkling, eye closure, widely smiling, whistling, and blowing air through puckered lips. The palsy may be temporary, recurrent, or permanent.

Extraoral Characteristics: The symptoms associated with Bell palsy depend on the extent of facial nerve involvement

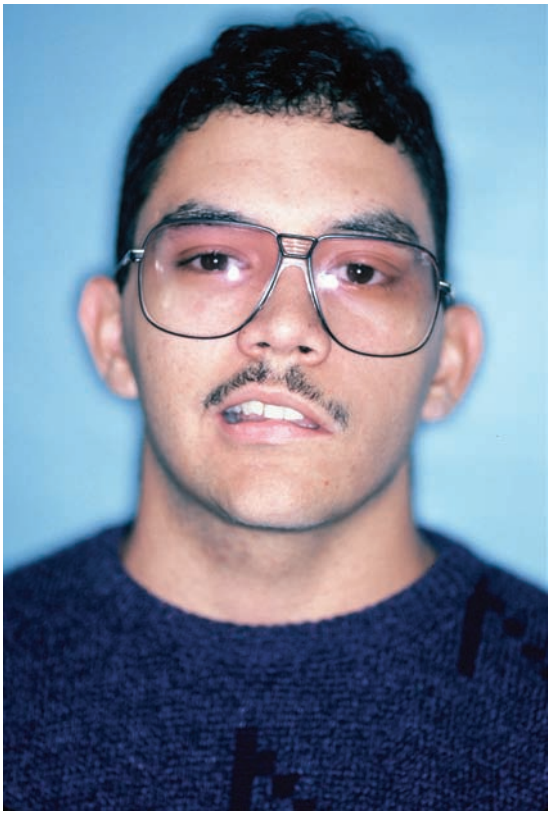

FIGURE 10.9. Bell palsy. This patient has paralysis of the left side of his face, affecting the muscles innervated by the facial nerve. (Courtesy of Dr. Carolyn Bentley.)

and can include keratoconjunctivitis sicca (dry eyes), posterior auricular pain, facial numbness, and **hyperacusis** (increased sensitivity to sound because of relaxed muscles in the ear). Normally, the individual is unable to completely close the eye and will roll the affected eye upward and inward in an attempt to do so (Bell phenomenon).

Perioral and Intraoral Characteristics: Patients are not able to smile and complain of drooling because of lip incompetence. Speech may be slurred, and mastication and swallowing may be impaired as well as the gag reflex. Nerves on the affected side may not provide stimulation to the salivary glands, resulting in diminished flow. If the patient is unable to keep the mouth closed, the oral environment will become even drier. Sensory loss, in addition to paralysis of the muscles innervated by the facial nerve, may result in taste disturbances or dysgeusia and a higher risk of infections from inadvertent trauma to the soft tissues.

Distinguishing Characteristics: None. Findings seen in Bell palsy can also be seen in stroke and other neurological problems affecting the facial nerve.

Significant Microscopic Features: Not applicable

Dental Implications: While safety glasses should be provided for all patients, it is especially important for patients with problems like Bell palsy, who cannot close their eyes completely. Patients should be given appropriate postoperative instructions after receiving local anesthetic on the nonaffected side, to avoid accidental trauma and choking. Diminished sensory input and compromised natural cleansing mechanisms result in food and debris accumulation in the affected side of the mouth. Nighttime xerostomia may be severe, and saliva substitutes and stimulants should be part of the preventive regimen. Together, these issues significantly increase caries risk and enhance caries activity, making frequent fluoride use essential. Patients with Bell palsy have an increased risk for periodontal diseases and should have frequent maintenance appointments to monitor their oral health. Treatment with corticosteroids increases the risk for fungal infections such as candidiasis. Refer to Clinical Protocol #4 for additional suggestions for managing xerostomia.

Differential Diagnosis: Facial features characteristic of this disorder may also be seen in other neurological disorders such as stroke.

Treatment and Prognosis: Most patients recover completely from Bell palsy within 3 to 6 months (NINDS, August 2011). Medical therapy depends on the suspected etiology of the condition but relies heavily on corticosteroids that, given as early as possible, have been found to offer the best chance for a complete recovery (Sullivan et al., 2007). Less than favorable outcomes occur in approximately 30% of patients, the majority of whom are usually over the age of 60 and exhibit total paralysis, hyposalivation, and taste disturbances. Performing surgical procedures on individuals with less than optimal recoveries has been successful in restoring more normal function to the tissues innervated by the facial nerve. Some of the procedures being used involve nerve grafting and relocation and muscle transfer from one area to another. In these cases, the patient has to train the new muscles and nerves to perform the appropriate motions needed to smile or close the eye (Taylor et al., 2011).

NAME: Trigeminal neuralgia

Etiology: Trigeminal neuralgia presents as excruciating pain in the tissues innervated by the trigeminal nerve. There are two forms of this condition: (1) idiopathic and (2) secondary. Idiopathic trigeminal neuralgia has no known cause. Secondary trigeminal neuralgia has been commonly associated with vascular anomalies and, less often, neoplastic growths that impinge, or put pressure, on the nerve, and inflammatory conditions. There is also an association between multiple sclerosis and trigeminal neuralgia, since trigeminal neuralgia occurs more frequently in individuals with multiple sclerosis (Singh et al., 2011).

Method of Transmission: Not applicable

Epidemiology: Approximately 15,000 cases of trigeminal neuralgia are identified in the United States every year (Singh et al., 2011). Twice as many females are affected as males, and most cases occur over the age of 40. It is

common for patients who have multiple sclerosis to also have trigeminal neuralgia (Singh et al., 2011).

Pathogenesis: The actual mechanism of producing a pain impulse is altered in this condition. Damage to the small and large nerve fibers is present, and it is thought demyelination of the axons permits uncontrolled transmission of pain impulses along the nerve fiber. The second or third divisions of the trigeminal nerve are most frequently affected, rarely both are affected, and involvement of the first division of the nerve is rarer. In most cases, the involvement is unilateral. Trigeminal neuralgia is considered a chronic condition, even though there may be intermittent remissions lasting several months at a time.

Extraoral Characteristics: There are no clinically observable signs of this condition; the major manifestation is pain, which is described as lightning-like, with impulses firing so quickly the patient often thinks it is constant instead of intermittent. A strange residual sensation may linger in the tissues after each episode. The pain is usually initiated by cutaneous contact with a particular trigger, such as touching a specific area, having cold or hot touch an area, air blowing on an area, chewing, yawning, and various food stimuli.

Perioral and Intraoral Characteristics: Intraoral mucous membrane stimulation may also trigger trigeminal neuralgia.

Distinguishing Characteristics: Chronic debilitating searing pain is characteristic of this disorder.

Significant Microscopic Features: Not applicable

Dental Implications: Patients may avoid dental care because they are afraid of initiating pain. All efforts should be made to identify and avoid pain triggers during dental treatment. Home care procedures may also be neglected for fear they will trigger painful episodes. Home care recommendations should be made after careful consideration of the needs of these patients. Patients should be referred to professionals who can help them cope with the full range of dental, medical, and psychologic problems accompanying this type of chronic pain disorder.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment is focused on preventing pain as opposed to stopping it once it starts, because the pain is of such short duration. Medical therapy consists of drug regimens including anticonvulsants, antidepressants, botulinum toxin (BOTOX) injections, and drugs that reduce painful nerve impulses. All of the drugs have been used with varying degrees of effectiveness. Surgery has been used to alleviate pressure on the nerve from arteries and growths. Substances have been injected into the ganglion to destroy those fibers associated with painful stimuli with good results. One highly effective therapy, gamma knife surgery, involves using high-energy photons aimed at the trigeminal nerve root to destroy specific parts of the nerve, thereby eliminating the pain (Singh et al., 2011).

There is no mortality associated with this condition; however, significant morbidity is common. The pain is reported as being severely intense, and its severity may be associated with the higher rate of suicides reported among people with this condition (Singh et al., 2011).

NAME: Migraine headache

Etiology: Migraine or vascular headaches are thought to be caused by a complex interaction between vascular and neural events, culminating in the classic signs of a migraine headache (Chawla et al., 2011).

Method of transmission: The method of transmission is unknown, but approximately 70% of those who experience migraines report having a first-degree relative (mother, father, sister, or brother) who also has migraines. This may indicate at the very least an inherited predisposition for the disorder (Chawla et al., 2011).

Epidemiology: An estimated 18% of women and 6% of men in the United States are reported to have migraine headaches (Porth, 2011).

Pathogenesis: Several theories exist, but at this time, migraines are considered to be the result of hyperexcitability of neurons in the cerebral cortex that, when further stimulated by a triggering event, leads to changes in blood flow to the brain. Triggering events vary widely but include stress, inappropriate sleep, medications, hormone fluctuations, smoking, bright lights, motion sickness, and certain foods such as aged cheese (Chawla et al., 2011).

Extraoral Characteristics: Migraines can occur with or without an **aura** (subjective symptoms that occur prior to the onset of a migraine headache). The headaches are usually unilateral and are described as throbbing or pulsating. Nausea, vomiting, photophobia, noise sensitivity, irritability, and malaise frequently accompany the headaches, which can last from a few hours to several days. Migraines with aura are preceded by some type of visual or other sensory disturbance. The usual visual disturbances reported are flashes of light, wavy lines obstructing the visual field, or blurred vision. Individuals experiencing migraines can be severely disabled by the symptoms.

Perioral and Intraoral Characteristics: Patients may report numbness in the face, lips, or tongue and speech or language disorders.

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: The dental implications associated with migraine headaches focus on managing the side effects of medications. Most medications being prescribed today have the potential to cause xerostomia. In addition, individuals who have frequent migraines and experience vomiting on a regular basis are at increased risk of dental erosion.

Frequent applications of topical fluorides at home and the use of products that will help to alleviate xerostomia are appropriate for these patients. See Clinical Protocol #4.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment usually depends on the severity of symptoms and amount of disability they cause. Medications are available that can reduce pain and limit the severity of any additional symptoms such as nausea and vomiting. In addition, prophylactic medications are given to reduce the frequency of the headaches. The prophylactic medications include antiepileptics, antidepressants, and antihypertensives (Chawla et al., 2011). Alternative therapies such as biofeedback, relaxation therapy, and stress reduction therapy have been successful in reducing the number of headaches for some individuals. Since each individual is different, the circumstances surrounding the creation of a migraine must be determined on an individual basis; therefore, much time is spent by the physician and the patient trying to identify what triggers that person's headaches.

NAME: Burning mouth syndrome

Etiology: **Burning mouth syndrome** (BMS) is an idiopathic condition that causes deep burning pain in the absence of any detectable dental or medical pathology for at least 4 to 6 months (Minor & Epstein, 2011). A diagnosis of BMS is usually made when all other etiologic possibilities for the symptoms have been ruled out. Refer to Box 10.5 for a list of disorders that may present with symptoms of BMS.

Method of transmission: Not applicable

Epidemiology: Prevalence of BMS is difficult to ascertain, but it is estimated that 0.7% of the population suffers from symptoms of BMS (Minor & Epstein, 2011). Most of those affected are women (7:1) during and after menopause; men appear to be affected at an older age (Gutkowski, 2004).

Pathogenesis: Although there have been many theories regarding the etiology of BMS, the general consensus at this time is that BMS is a form of neuropathy resulting in chronic pain (Minor & Epstein, 2011).

BOX 10.5

Conditions Associated with Burning Sensations in the Oral Mucosa

- Xerostomia
- Vitamin deficiencies
- Mineral deficiencies
- Gastrointestinal (GI) disorders
- Fungal infections
- Hormone deficiencies
- Neurologic problems
- Blood diseases
- Allergic and inflammatory disorders
- Adverse effects of drugs
- Psychologic disorders
- Phantom pain

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: The most important clinical feature of this disorder is that there are no clinically observable abnormalities present. There are no mucosal changes or functional changes, and nothing seems to be out of order, except the individual is reporting a burning sensation, often severe, in the oral tissues. The burning occurs most often in the anterior two-thirds of the tongue, the anterior hard palate, and the mucosa of the lower lip (Grushka et al., 2002). Typically, there is an absence of symptoms during sleep, and the symptoms are less severe in the morning but increase as the day progresses. Other oral symptoms associated with BMS are intermittent xerostomia and taste perversions (abnormal taste sensations).

Distinguishing Characteristics: Burning sensations in the oral soft tissues without evidence of identifiable pathology

Significant Microscopic Features: Not applicable

Dental Implications: Patients who present with this disorder should be reassured that they are in fact experiencing pain even if there are no clinically observable signs. The dental professional should be willing to suggest a referral to a physician or mental health professional if treatment offered does not appear to result in any relief of symptoms.

Differential Diagnosis: Refer to Box 10.5.

Treatment and Prognosis: The most important element in successfully treating this disorder is to identify the cause, if possible, and eliminate it. Complete blood counts, allergy testing, tests to determine nutritional status, and oral cultures or biopsies should be done to try to determine the exact cause of the sensations. If all other possibilities are ruled out and BMS is the most likely diagnosis, there are several treatments that have shown varying degrees of success. Medical treatment with clonazepam and paroxetine has shown the most promise, with cognitive behavioral therapy and counseling therapies also proving to be helpful (Minor & Epstein, 2011). The patient should be advised to avoid mouth rinses containing alcohol or cinnamon flavoring as well as tobacco products, since these substances may increase the level of discomfort. Chewing on ice chips and chewing sugar-free gum may alleviate the symptoms for short periods of time. BMS may persist for years with no relief, become episodic, and then disappear altogether, or it may never resolve.

Skeletal System Disorders

Several skeletal disorders should be discussed for the simple reason that they are among the most common chronic diseases known to mankind. Osteoarthritis or rheumatoid arthritis (RA) affects almost 100% of the population at some point in their lives. Osteoporosis is a major preventable health problem for women and men. Paget disease and fibrous dysplasia (FD), even though uncommon, have specific oral implications and manifestations. The dental hygienist will have to manage disorders of the

temporomandibular joint (TMJ) on a daily basis, not only because of the need to identify patients with symptoms but also to be able to modify treatment procedures to put as little stress as possible on the joint.

NAME: Osteoarthritis

Etiology: Osteoarthritis affects the joints, specifically the articular cartilage and bone directly underneath it. It is considered to be a multifactorial degenerative disease with both genetic and environmental risk factors (Porth, 2011). Some of the risk factors include trauma, repetitive use, infection, age, obesity, neuropathy associated with diseases such as diabetes, and orthopedic and bone disorders. Many feel that it is due to excessive wear and tear on the joints, but often, there is no trauma associated with its occurrence.

Method of transmission: Genetic risk factors may be transmitted; otherwise, this is not transmissible.

Epidemiology: Osteoarthritis is widespread; it is estimated that 80 to 90% of the US population over the age of 65 have evidence of this disease (Lozada et al., 2012). It affects all races, and women are more susceptible to some forms of the disease than are men. By the age of 75, almost 100% of both men and women show some signs of osteoarthritis (Lozada et al., 2012).

Pathogenesis: The underlying pathology in osteoarthritis is the destruction of cartilage covering the articular surfaces of bones in synovial joints, with opposing bones eventually rubbing directly on each other because there is so little cartilage. During this process, small pieces of cartilage break away and float freely in the joint space, causing more impairment of joint function. In response to the destructive process, the body forms new bone at the margins of the joint called bone spurs, or **osteophytes,** which cause additional impairment of joint function. Finally, the bone underlying the articulating surfaces collapses, causing severe limitation of motion with accompanying pain.

Extraoral Characteristics: The joints of the fingers and the weight-bearing joints such as the knee, hip, and sometimes the cervical and lumbar (lower) regions of the spine are affected most often. The pain associated with osteoarthritis has been characterized as a deep, achy joint pain that increases as the joint is used. Small pea-sized areas of exostosis, or bony outgrowth, are seen in the joints of the fingers. These areas are called Heberden nodes and are seen often in women but seldom in men (Fig. 10.10).

Perioral and Intraoral characteristics: Degenerative changes in osteoarthritis are commonly seen in the TMJ and result in crepitus, deviation, deflection, and limitation in joint movement. TMJ dysfunction is discussed later in this chapter.

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

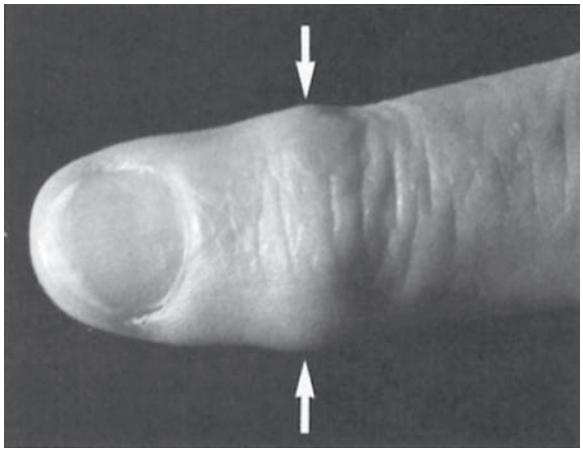

FIGURE 10.10. Heberden nodes. These are characteristic of the joint deformities (*arrows*) seen in the hands of individuals with osteoarthritis. (From Bickley LS, Szilagyi P. Bates' guide to physical examination and history taking. 8th ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

Dental Implications: Treatment modifications might include adapting the patient's position for comfort, keeping appointments short, and scheduling appointments at a time when the patient is feeling best. Methods to manage excessive bleeding during dental/dental hygiene procedures should be planned, since many medications used to treat osteoarthritis have an anticoagulant effect. Patients with total joint replacements may require prophylactic antibiotic coverage prior to dental procedures to prevent a hematogenous joint infection. Refer to Application 10.3 for a discussion about prophylactic antibiotic coverage for patients with total joint replacements. The dental hygienist may have to recommend modifying home care implements, making them easier to hold, to enable patients to effectively remove dental biofilm from their teeth. Mechanical toothbrushes are especially helpful for this population.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment of osteoarthritis focuses on relieving the symptoms and rehabilitative measures, which attempt to enhance the supporting structures of the joints. Resistance training exercises and exercising with weight partially removed from the joint, as occurs in water aerobics, has been found to be very helpful. Medications that reduce inflammation and pain, such as NSAIDs and other anti-inflammatories, are important. Injection of sodium hyaluronate (a substance that mimics the actions of synovial fluid) directly into the joint space appears to help lubricate the joint and provides temporary comfort for many patients. When all else fails to provide relief, surgery is considered. Some forms of surgery simply remove the floating bodies or spurs around the joints; others actually remodel the bone surfaces. In the case of hip or knee osteoarthritis, the joint may eventually need to be replaced.

NAME: Rheumatoid arthritis (RA)

Etiology: RA is a chronic systemic inflammatory disease with a multifactorial etiology. Genetic factors comprise

APPLICATION **10.3**

Prophylactic Antibiotic Coverage to Prevent the Hematogenous Spread of Infection in Total Joint Replacements

The American Association of Orthopaedic Surgeons (AAOS) released an informational statement on this topic in February 2009 and a revised statement on the same topic in June of 2010. The full statement is available at *http://www.aaos.org/about/papers/advistmt/1033.asp*. In short, the statement recommends prophylactic antibiotic coverage for "all patients with a prosthetic joint replacement" (AAOS, 2010). It further states, "Any perceived benefit of antibiotic prophylaxis must be weighed against the known risk of antibiotic toxicity, allergy, and development, selection and transmission of microbial resistance. Practitioners must exercise their own clinical judgment in determining whether or not antibiotic prophylaxis is appropriate" (AAOS, 2010). The prophylactic regimen recommended for dental treatment follows:

- Two grams of cephalexin, cephradine, or amoxicillin given by mouth 1 hour prior to the procedure

The dental community has voiced confusion and surprise in response to these recommendations. Some say there is little or no evidence to support this position, while others are apt to agree with the AAOS (Olsen et al., 2010). Remember also, that the American Heart Association has just recently reduced the number of conditions for which it recommends antibiotic prophylaxis prior to dental treatment to just conditions associated with the highest risk of developing infective endocarditis. The controversy continues, but right now, the decision of whether or not to provide antibiotic prophylaxis rests with each dental health care practitioner.

50% of the risk for developing RA; other risk factors include infectious agents such as Epstein-Barr virus, sex hormones, and immunologic factors (Temprano & Smith, 2011).

Method of transmission: RA has a strong genetic component; otherwise, it is not transmissible.

Epidemiology: RA affects approximately 3 of every 10,000 individuals; it affects all races and all age groups. Females are three times more likely to have RA than men, and the peak age at onset is between the ages of 35 and 50 years (Temprano & Smith, 2011).

Pathogenesis: RA is primarily a disease of the joints, but it can also affect any organ, such as the heart or the skin. The inflammation starts in the synovial membrane that lines the joints. The membrane thickens and extends into the joint cavity, often filling the space. The inflammation also affects the articular cartilage on the ends of the bones, causing the formation of scar tissue between the bones. Calcification of the scar tissue causes ankylosis, or fusion of the bones, resulting in the characteristic crippling of the hands (Fig. 10.11). The hands and the feet are affected most often, but other joints (hip, knee, shoulder, and TM) are usually not spared. The spine often becomes involved as the disease becomes more advanced.

Extraoral Characteristics: Pain is the presenting feature of this disorder. Morning stiffness and soft tissue swelling or accumulation of fluid around the joints are also characteristic. There is no bony overgrowth as in osteoarthritis. Rubbery nodules or rheumatoid nodules may be found under the skin at pressure points such as the elbow. These are granulomatous lesions that develop around small blood vessels (Porth, 2011) (Fig. 10.12). Rheumatoid nodules may or may not be painful. Other organ manifestations of the disease include fluid accumulation around the heart and in the lungs, entrapment of nerves in the deformities caused

FIGURE 10.11. Rheumatoid arthritis. The hands of a patient with advanced rheumatoid arthritis show swelling of the joints and the classic ulnar deviation of the fingers. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

FIGURE 10.12. Rheumatoid nodule. Several large rheumatoid nodules can be seen on the elbow of this elderly patient. (Image provided by Stedman's.)

FIGURE 10.13. Rheumatoid arthritis. Open-bite malocclusion due to condylar resorption. Koopman WJ, Moreland LW, Arthritis and allied conditions: a textbook of rheumatology. 15th ed. Philadelphia: Lippincott Williams & Wilkins, 2005.)

by RA such as carpal tunnel syndrome, and keratoconjunctivitis sicca (dry eyes). RA may be the connective tissue disorder associated with secondary Sjögren syndrome.

Perioral and Intraoral Characteristics: RA is associated with xerostomia and TMJ dysfunction. Joint destruction can be extensive and lead to functional limitations, malocclusion (Fig. 10.13), and severe pain.

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: The dental hygienist should pay careful attention to the drug history of the patient with RA because of the possibility of immunosuppression from long-term use of disease-modifying antirheumatic drugs (DMARDs) and corticosteroids (discussed in the next section). Long-term steroid use is also associated with a significant decrease in bone density that can affect the mandible and the maxilla. Blood clotting may be affected by drugs used to treat RA, making it important to determine the individual's bleeding time, especially prior to procedures during which bleeding is anticipated. Patients with total joint replacements may require prophylactic antibiotic coverage prior to dental procedures to prevent a hematogenous joint infection. Refer to Application 10.3. Appointment modifications that might make dental treatment more comfortable include scheduling short appointments, modifying the patient's position in the chair, providing pillows or rolled up towels to support joints, and using bite blocks to assist in keeping the mouth open comfortably. Examination of the TMJ for RA manifestations is important to plan interventions to limit destruction in this joint. Home care procedures and instruments might need to be modified to contend with dexterity problems caused by destruction of the joints of the fingers and hands. Finally, many of the drugs given for RA have the potential to cause xerostomia; therefore, preventive strategies for caries and periodontal disease should be initiated early, before any disease can occur.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment of RA focuses on slowing the progression of the disease and minimizing the deformities caused by it. Medications, exercise, and rest are all essential components of controlling this disease. Exercises focus on strengthening the support system for the joints and maintaining flexibility. Medications that interfere with the disease process, called DMARDs, are the mainstay of modern drug therapy. Methotrexate, a strong immunosuppressive drug, is the DMARD of choice at this time. Other DMARDs include medications that inhibit the binding of TNF to cell surface receptors and those that reduce the infiltration of inflammatory cells into an inflamed area and thus decrease inflammation. These are often combined with anti-inflammatory drugs (corticosteroids and NSAIDs) and analgesic (acetaminophen) drugs to provide the highest level of comfort and function. Surgical treatment may be indicated including joint fusion and total joint replacement among others.

The disease usually follows an episodic course with many exacerbations and remissions over the years. Approximately 40% of individuals with RA become significantly disabled after 10 years, and they have a higher mortality rate than someone without RA (Temprano & Smith, 2011).

NAME: Osteoporosis

Etiology: Osteoporosis is a skeletal disorder characterized by low bone density and deterioration of the structure of the bone, leading to an increased risk of fractures. There are two types of osteoporosis: (1) primary and (2) secondary. Primary osteoporosis is seen in postmenopausal women and in the elderly of both sexes. There does not seem to be a clear cause of primary osteoporosis, but there are many risk factors that increase an individual's chance of having osteoporosis. Box 10.6 lists some of these risk factors. Individuals who do not have osteoporosis but have low bone density compared to the norm are said to have osteopenia. Many of those with osteopenia progress to osteoporosis. Secondary osteoporosis is associated with a known cause, which is

BOX 10.6 Risk Factors for Osteoporosis

- Female
- Age
- Low body weight/small bones
- Family history
- Physically inactive
- Estrogen deficiency/postmenopausal
- White/Asian
- Certain medications
- Previous fractures
- Low calcium/vitamin D intake
- Tobacco use
- Alcohol abuse
- Excessive caffeine ingestion
- Drugs (anticonvulsants, heparin, corticosteroids)
- Diseases (diabetes, Cushing, celiac, anorexia nervosa, rheumatoid arthritis [RA])

often an endocrine disorder or the use of certain medications, such as corticosteroids, for long periods of time.

Method of Transmission: Not applicable

Epidemiology: The National Osteoporosis Foundation estimates that 10 million Americans already have osteoporosis, and another 33.6 million have osteopenia. Eight million women and two million men are affected. They also estimate that 1 of every 2 women and 1 of every 5 men will have an osteoporotic fracture during their lifetimes (NOF, 2010).

Pathogenesis: The pathology associated with all forms of osteoporosis is the result of defective bone remodeling. Bone is not a static tissue and is simultaneously undergoing formation and resorption on a continual basis. When the resorption of bone exceeds the formation of bone, the density of the bone decreases as does the quality of the bone. Figure 10.14 compares normal bone structure to osteoporotic bone.

Extraoral Characteristics: Some of the clinical findings associated with osteoporosis are a decrease in height of between 10 and 15 cm, dowager hump (curvature of the upper back), lower back pain, and bone fracture caused by minimal trauma such as coughing. Osteoporosis is considered a "silent" disease. Individuals may not know they have it until they experience a fracture or one or more of the other signs and symptoms.

Perioral and Intraoral Characteristics: Osteoporosis can be seen in the maxilla and the mandible as loss of trabecular detail and thinning of the cortical bone. Research has suggested a link between osteoporosis and accelerated progression of bone loss due to periodontal infection. The use of bisphosphonates and other antiresorptive drugs, which reduce osteoclast activity and increase bone density, to treat osteoporosis has been associated with **osteonecrosis** (pathologic death of the bone) of the mandible (AAE, 2010).

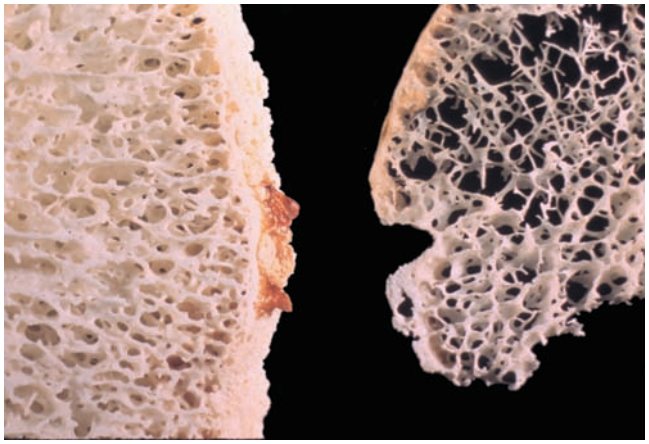

FIGURE 10.14. Osteoporosis. Bone from the femur of an 82-year-old female with osteoporosis **(right)** compared with a normal bone cut to the same thickness **(left)**. (From Rubin E, Farber JL. Pathology. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2005.)

Distinguishing Characteristics: Not applicable

Significant Microscopic features: Characteristic low mineral density as seen in Figure 10.14

Dental Implications: Maintaining periodontal health should be stressed in patients who have been identified as having osteoporosis because of the possibility of accelerated bone loss. In addition, those taking bisphosphonates or other antiresorptive drugs should be advised to report any pain or swelling in either jaw, infections that produce pus, change of sensation within the jaws, and ulceration of the mucosa covering the jaws that does not heal, all of which may be associated with osteonecrosis of the jaw (AAE, 2010). See Application 10.4 for more information.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Treatment focuses on maintaining the current level of bone density through weight-bearing exercises combined with resistance training. Increasing the dietary intake of calcium as well as vitamin D are crucial elements of treatment and prevention. Drugs used to treat osteoporosis include bisphosphonates and calcitonin that increase bone density by reducing the activity of osteoclasts, parathyroid hormone that actually increases the formation of bone, and estrogen replacement therapy that decreases the bone density loss associated with menopause. Estrogen use has been associated with a higher rate of some cancers in women and is very controversial at this time. Prevention is the key to controlling this disease and should begin in childhood with the formation of healthy eating habits, maintaining an active lifestyle, and avoiding tobacco use. Prevention should not begin at age 50 when an individual is diagnosed with osteoporosis or osteopenia; however, it is never too late to try to stay healthy and active.

NAME: Paget disease (osteitis deformans)

Etiology: Paget disease is a skeletal disorder characterized by bone resorption followed by excessive growth of defective bone. The etiology of Paget disease is unknown, but genetic and environmental factors have been suggested.

Method of Transmission: Approximately 15 to 40% of individuals with Paget disease have a first-degree relative who also has the disease, suggesting a possible genetic predisposition (Porth, 2011).

Epidemiology: Approximately 1 to 3% of the US population is affected by this disease. More males than females are affected. The disorder rarely occurs under the age of 25, with most cases occurring after the age of 60 (Lohr & Driver, 2011).

Pathogenesis: Initially, the disease causes excessive resorption of the cancellous bone, which is replaced with a vascular connective tissue. After the initial resorption, new bone is created at a very fast rate, causing enlargement of the affected bones. The new bone is abnormal in structure, causing it to be weaker than normal bone, even though

APPLICATION **10.4**

Antiresorptive Agent–Induced Osteonecrosis of the Jaw (ARONJ)

Osteonecrosis is the term used to describe a condition in which the bone dies or undergoes necrosis. This condition has long been associated with exposure of the bone to ionizing radiation used to treat malignant growths (osteoradionecrosis). During radiation therapy, the capacity of the bone to repair itself and recover from infections or trauma is permanently altered by the damage done to bone cells and structures supplying nutrients to the bone. Similarly, bisphosphonates and some other antiresorptive agents alter the balance of normal bone turnover by decreasing the number of osteoclasts allowed to become active and by causing premature apoptosis (natural death) of already functioning osteoclasts. This causes the inhibition of normal bone remodeling and formation that could result in a decreased ability of the bone to repair itself. This is thought to be the process associated with the development of what the American Dental Association (ADA) now calls antiresorptive agent-induced osteonecrosis of the jaw, or ARONJ (Hellstein et al., 2011; Blanchart & Harris, 2011).

Since 2003, cases of ARONJ have been reported among patients who are taking intravenous bisphosphonates to prevent bone loss associated with cancer therapy and with some other chronic conditions, such as Paget disease. In 2006, cases of ARONJ began to be reported among individuals taking oral bisphosphonates to treat or prevent osteoporosis (Hellstein et al., 2011). In light of the fact millions of individuals are taking this medication for the prevention of osteoporosis, the dental community has taken steps to address the problem and determine the direction of further research.

Patients who are undergoing IV therapy for cancer with bisphosphonates have the highest risk for developing ARONJ (Hellstein et al., 2011). Individuals taking oral bisphosphonates have a very low risk of ARONJ. The current data suggest that the incidence (rate at which new cases develop) is less than 1 case per 100,000 person-years of exposure (the risk increases the longer the medication is taken) (Blanchart & Harris, 2011). ARONJ is often asymptomatic and may be present for weeks or months before being noticed by the patient. Symptoms include pain, soft tissue swelling, infection and drainage, tooth mobility, halitosis, and exposed bone. Sometimes, the symptoms will mimic other dental problems such as tooth abscesses and periodontal infections, but they never totally resolve even with optimal treatment. ARONJ can occur spontaneously, but it usually is preceded by some sort of dental trauma such as an extraction or chronic irritation associated with denture wear. Dentists and dental hygienists should note the use of antiresorptive drugs by their patients and the presence of other factors that may place patients at a higher risk for developing ARONJ (such as age over 65, presence of periodontal disease, use of antiresorptive drugs for more than 2 years, smoking, diabetes, and wearing dentures) when determining the cause of symptoms such as those listed above (Hellstein et al., 2011).

The ADA has developed some general recommendations for managing patients who are taking antiresorptive drugs (Hellstein et al., 2011):

- Provide patients who have not had regular dental care with a comprehensive examination before or early in therapy.
- Schedule regular dental examinations during therapy
- Stress maintenance of healthy oral tissues with good oral hygiene practices
- Advise patients to contact their dentist if any problems are observed in the mouth
- Minimize surgical manipulation; for example, endodontic therapy may be preferable to tooth extraction.
- Perform surgery in a localized area to observe healing before performing more extensive surgery; for example, perform periodontal surgery in one quadrant and observe healing for at least 2 months before completing the entire mouth
- Prescribe rinsing with chlorhexidine twice daily during the 2-month recovery period, and prescribe both pre- and post-surgery oral antibiotics

Dental practitioners should fully discuss and disclose the risk for ARONJ when obtaining informed consent before performing specific dental procedures associated with an increased risk for ARONJ. Suggestions for information to be included in such a discussion are available in the ADA ARONJ report, which can be accessed via the link at the end of this application.

The area in Figure 10.15 was discovered in a 66-year-old, 5-ft 3-in tall, 102-lb, white female patient who presented to the dental hygiene clinic with severe oral pain. Her medical history included severe rheumatoid arthritis (RA) of over 10 years' duration and secondary Sjögren syndrome. Her current medications included methotrexate (an antineoplastic agent used to treat RA), an NSAID (for reduction of pain and inflammation), an antimalarial (used to treat RA), bisphosphonates (used to treat osteoporosis), thyroid medication (for thyroid disease), calcium (for osteoporosis), and a proton pump inhibitor (used to reduce the risk of gastric ulcer development in patients taking nonsteroidal anti-inflammatory drugs [NSAIDs]).

FIGURE 10.15. Antiresorptive agent–induced osteonecrosis of the jaw. An area of necrotic bone is visible in the interproximal area between 21 and 22.

(*continued*)

APPLICATION 10.4 *(continued)*

Clinical examination revealed an area of necrotic bone in the interproximal area between teeth 21 and 22. The surrounding soft tissue was erythematic and swollen and bled easily. There was a corresponding area of necrotic bone on the lingual interproximal surface. The patient was referred to an oral medicine clinic at an area dental school for diagnosis and initial therapy. The initial diagnosis was bisphosphonate-associated osteonecrosis, and the initial therapy consisted of careful debridement of the area, topical alcohol-free antibacterial rinses, and a course of systemic antibiotics. The patient was to be monitored closely. The patient was not seen again at the dental hygiene clinic, but a report stating the patient had achieved full resolution of the lesion was received about 5 months later.

These Web sites are recommended to keep abreast of the most current information regarding ARONJ.
American Dental Association: *http://www.ada.org/sections/professionalResources/pdfs/topics_ARONJ_report.pdf*
National Osteoporosis Foundation: *http://www.nof.org/home*
American Society for Bone and Mineral Research: *http://www.asbmr.org*

it is highly mineralized. The bones of the spine, skull, sternum, pelvis, and femur are affected most often, but any bone can be affected. In addition to these problems, approximately 5 to 10% of severely affected individuals will develop osteogenic sarcoma within the bone lesions (Porth, 2011).

Extraoral Characteristics: Involvement of the spine can cause neurologic symptoms ranging in severity from transient pain to complete paralysis due to compression of the spinal cord. When the disease affects the femur, it causes severe bowing and is associated with increased incidences of stress fracture. Radiographs will show enlargement of the bones, with areas of excessive mineralization appearing as radiopaque patches resembling "cotton wool" (Fig. 10.16). Diagnosis of Paget disease is based on the results of blood tests that show significantly elevated levels of alkaline phosphatase and radiographic manifestations.

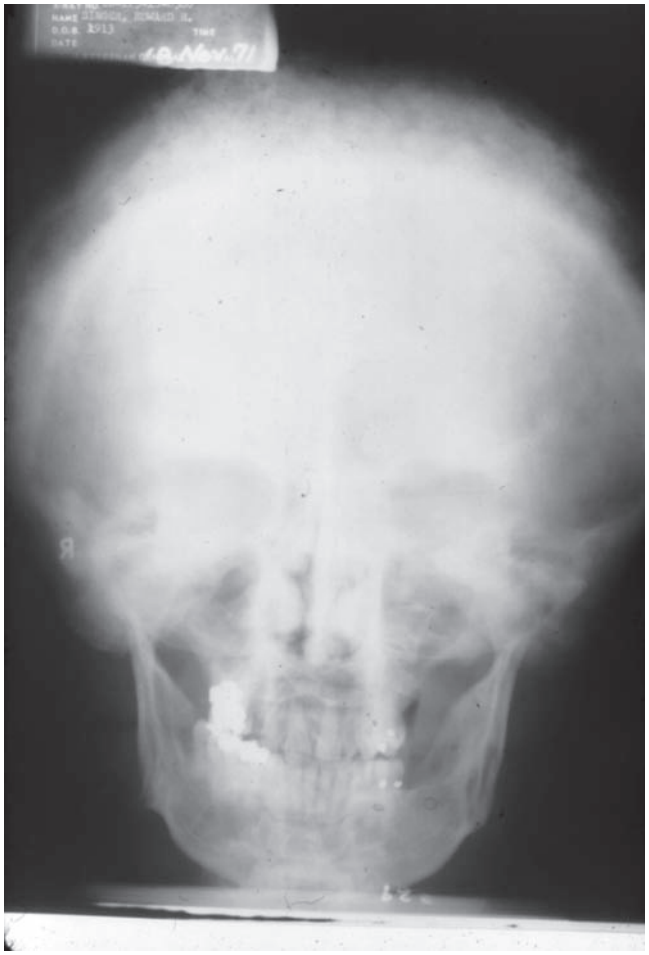

FIGURE 10.16. Paget disease. Radiograph showing the cotton-wool appearance of the bone in Paget disease. Note the involvement of the mandible. (Courtesy of Dr. William Carpenter.)

Perioral and Intraoral Characteristics: Involvement of the skull usually results in asymmetric enlargement of the occipital and frontal bones (Fig. 10.17). Depending on the extent of the deformity, neurological symptoms can range from mild headache to dementia. Excessive bone growth around the foramina of the skull can lead to cranial nerve compression and blindness, deafness, constant vertigo, impaired motor function, and more. Maxillary and/or mandibular involvement results in bilateral enlargement of the jaw with increased tooth spacing and malocclusion (Fig. 10.18). Patients may complain that removable prosthetics no longer fit and they can no longer close their lips. They may also complain of temporomandibular dysfunction. Loss of the lamina dura and periodontal ligament space

FIGURE 10.17. Paget disease. Asymmetric enlargement of the skull bones can cause neurologic problems, and bone growth can encroach on the foramina, putting pressure on the nerves and vessels passing through them. (Courtesy of Dr. William Carpenter.)

FIGURE 10.18. Paget disease. Malocclusion caused by enlargement of the maxilla. Note the normal size of the mandible. (Courtesy of Dr. William Carpenter.)

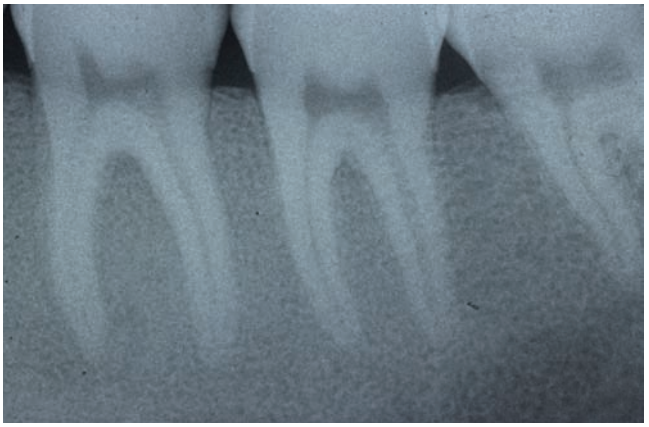

FIGURE 10.19. Fibrous dysplasia. Radiograph of the mandible showing the characteristic ground-glass appearance of the bone in fibrous dysplasia. (Courtesy of Dr. Charles Dunlap.)

as well as **hypercementosis,** or the growth of excessive amounts of cementum, in addition to the cotton-wool appearance of the affected bone, may be present in intraoral and panoramic radiographs.

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Not applicable

Dental Implications: Dental management of the functional problems associated with malocclusion and TMJ dysfunction caused by Paget disease is one challenge presented by these patients. Pain management may become an issue if nerves are impinged upon by thickening bone. In addition, antiresorptive drugs are used to treat Paget disease, and patients should be advised about the possibility of ARONJ.

Differential Diagnosis: Not applicable

Treatment and Prognosis: Often, the disease is localized and self-limiting and requires no treatment. Otherwise, treatment is determined by the severity of the symptoms and the extent of the involvement. Some of the same drugs used to treat osteoporosis are used to treat Paget disease, specifically the bisphosphonates, which inhibit bone loss by decreasing bone resorption and by slowing the formation of new bone.

The prognosis for individuals with Paget disease is excellent in cases that are treated appropriately. When osteogenic sarcoma is diagnosed, the prognosis is poor, with most succumbing to the illness within 3 years of diagnosis.

NAME: Fibrous dysplasia

Etiology: A defective gene produces increased levels of a specific protein that enhances the action of certain cells including osteoblasts and fibroblasts resulting in FD.

Method of Transmission: The defective gene is neither inherited from the parent nor passed on to the person's children (FDF, No date). One rare form of the disease, cherubism, is an autosomal dominant genetic disorder.

Pathogenesis: Spongy bone is replaced by fibrous tissue, which precedes the formation of immature woven bone. The woven bone exhibits a characteristic "ground-glass" radiographic appearance (Fig. 10.19). Several forms of this disease are discussed below.

Extraoral Characteristics:

- Monostotic FD occurs in only one bone, usually one of the ribs, femur, tibia, or craniofacial bones. This form of the disease accounts for most of the cases and may present with bone pain and pathologic fractures or may be asymptomatic. Diagnosis is usually made between the ages of 10 and 30 years (Gannon, 2012).
- Polyostotic FD occurs in multiple bones including the skull, facial bones, pelvis, spine, and shoulder girdle. Symptoms of pain, swelling, and spontaneous fracture may be the presenting features of this form of the disease. Over time, the weight-bearing bones of the hip, if affected, will become deformed or bowed. More females are affected than males (Rubin et al., 2012).
- McCune-Albright syndrome consists of polyostotic FD, cutaneous hyperpigmented areas called café au lait macules with characteristic jagged borders (Fig. 10.20), and one or more endocrine abnormalities. The most common endocrine abnormality is precocious or very early sexual development. Other abnormalities that may be present include diabetes, hyperthyroidism, hyperparathyroidism, and acromegaly. Oral manifestations including partial anodontia may be present in some cases.
- Jaffe-Lichtenstein syndrome consists of polyostotic FD and the cutaneous café au lait macules without any endocrine abnormalities.

Perioral and Intraoral Characteristics: Jaw involvement is common in the monostotic form of FD, the maxillae is affected more often than the mandible, and the clinical presentation is one of slow enlargement of the bone, creating facial asymmetry. Cherubism is a rare inherited form of FD that affects the bones of the face, especially

FIGURE 10.20. Café au lait macule. This café au lait macule was observed on the abdomen of a patient with McCune-Albright syndrome. Note the jagged border, which is characteristic of the café au lait macules seen in fibrous dysplasia. (Courtesy of Dr. Michael Brennan.)

the mandible and, less often, the maxilla. Replacement of spongy bone with fibrous tissues gives the area of the cheeks a very swollen appearance (Fig. 10.21). This form of FD is not painful. If the bones of the inferior orbit enlarge, the eyes appear to tilt upward like the eyes of cherubs in religious paintings. Oral problems are encountered with this form of the disorder. Affected individuals have premature loss of primary teeth and failure or delayed eruption of the permanent teeth. In addition, the teeth may be malformed and out of place or missing (partial anodontia), resulting in severe malocclusion (Fig. 10.22). The characteristic radiographic appearance of cherubism presents as multiple, well-defined, multilocular, radiolucent lesions scattered within the affected bones (Fig. 10.23). The cortical bone thins and may become perforated.

FIGURE 10.21. Cherubism. This 4-year-old female exhibits the facial features characteristic of cherubism, including the swollen appearance of the cheeks. (Courtesy of Tirza Jo.)

FIGURE 10.22. Cherubism. Intraoral photograph of the same female shows partial anodontia and malocclusion affecting both the mandible and the maxilla. (Courtesy of Tirza Jo.)

The disease is self-limiting and progresses rapidly during childhood, but slows during and after puberty, and normally regresses or resolves by the age of 30, leaving no permanent disability or disfigurement other than the malocclusion.

Distinguishing Characteristics: The facial features of cherubism are characteristic early in life but resolve as the child grows.

Significant Microscopic/Radiographic features: The ground-glass appearance of the woven bone on radiographs is characteristic of FD.

Dental Implications: Patients with cherubism require intensive intervention and long-term management of their dental and oral health. Most children will require interventional and anticipatory orthodontic therapy throughout childhood to manage missing teeth and delayed eruption patterns in order to prepare for permanent treatment after they have reached their optimum growth. These options may include removable or fixed appliances and, if appropriate, implants.

Treatment and Prognosis: Treatment, other than follow-up and biopsy, is usually unnecessary for small lesions, especially those of the monostotic type. Larger lesions and the multiple lesions of polyostotic FD are often treated with surgical recontouring after the individual has reached adulthood to decrease the chance for recurrence. Very often, hip deformities cause mobility problems and result in the need to use a wheelchair. Individuals with McCune-Albright syndrome need to be treated for their endocrine abnormalities. In addition, there is a very slight chance (0.4 to 4%) that the fibrous lesions can undergo a malignant transformation. This has been reported more often in the polyostotic form and in individuals who have a history

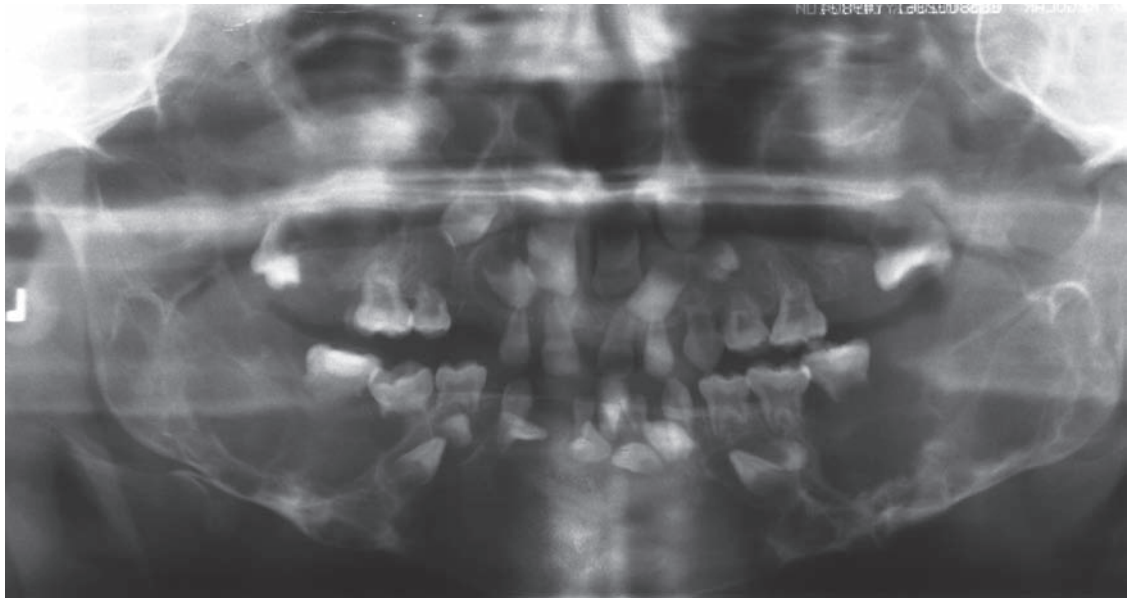

FIGURE 10.23. Cherubism. Panoramic radiograph of the same female showing partial anodontia, malformed teeth, and multiple well-defined, multilocular, radiolucent lesions scattered throughout the mandible and maxilla. (Courtesy of Tirza Jo.)

of radiation treatment for their lesions. Radiation treatment is no longer considered appropriate therapy for this disorder.

Temporomandibular Joint Disorders

The TMJ consists of the mandibular condyle, which fits into the mandibular fossa of the temporal bone, the articular disk and the ligaments that support the joint. The joint is separated into upper and lower synovial cavities by the articular disk and is surrounded by ligaments that protect the joint and limit motions that could damage it. The muscles of mastication, while not part of the joint, are intimately involved with proper joint function.

NAME: Temporomandibular disorder

Etiology: Temporomandibular disorders (TMDs) are a group of disorders characterized by functional impairment or pain related to the TMJ. These include disorders related to the bone, ligaments, and articular disk of the joint and to the associated muscles of mastication. See Box 10.7 for a classification of TMDs. The most common cause of dysfunction is acute or chronic trauma. Sudden, forceful trauma such as a blow to the jaw is considered acute, while chronic trauma may take the form of clenching and bruxing. Occlusal conditions that cause deviant or traumatic muscle function such as an anterior open bite, a significant overjet, and five or more nonreplaced missing teeth have been associated with an increase in TMDs (Okeson, 2003). Emotional stress is associated with an increase in muscle tone and unconscious muscle function, which may cause an increase in parafunctional habits (masticatory motions not related to the act of eating such as bruxing or chewing on pens). Patients who complain of chronic mouth, ear, sinus, and, sometimes, cervical neck pain also have a higher risk of developing TMD because the body protects the painful area by limiting its function. Muscles in these areas may undergo significant change because of deviant use or nonuse.

Method of Transmission: Not applicable

Epidemiology: Numerous studies have reported TMD signs and/or symptoms in up to 75% of the population. However, only about 5 to 10% reported enough pain

BOX 10.7 Classification of Temporomandibular Disorders (TMDs)

- Muscle disorders
  - Myofascial pain disorder
  - Local myalgia
- TMJ disorders
  - Disk derangement (articular disk out of place, with or without reduction)
  - Inflammation of the articular surfaces
    - Osteoarthritis
    - Rheumatoid arthritis
- Ankylosis or fixation (hypomobility)
  - Trismus
- Joint laxity (hypermobility)
- Trauma
- Defective coronoid process
- Growth disorders
  - Bone
    - Agenesis
    - Hypoplasia
    - Hyperplasia
  - Muscles
    - Hypotrophy
    - Hypertrophy

and/or dysfunction to seek care. TMDs occur more frequently between 20 and 40 years of age and significantly more females (4:1) than males seek care for the symptoms (Okeson, 2003; Guardia & Berman, 2012).

Pathogenesis: The pathogenesis of the condition depends on the specific cause. For example, in an acute traumatic event such as a sharp, forceful blow to the jaw, the tissues of the joint will show signs of inflammation (swelling, pain, tenderness to touch and warmth). The range of motion or opening may be limited and the teeth may not occlude normally, due to swelling in the joint. With time and proper treatment, the inflammation resolves and the joint returns to normal with no permanent damage. On the other hand, chronic trauma follows a more insidious or gradual course. For instance, someone missing all of their molars will have to learn how to chew on the anterior and premolar teeth; because the TMJ is not made to function heavily on these teeth, it must attain an abnormal position to do so which over time causes significant TMJ damage. In addition, the muscles of mastication will have to function out of their normal range of motion. The chronic trauma induced by these functional changes may lead to permanent joint damage. Growth disorders can cause either unilateral or bilateral, hyperplastic or hypoplastic development of the joint. These disorders can affect the condyle, coronoid process, and/or the TMJ itself. Acromegaly is an example of a growth disorder that can result in unbalanced jaw development and TMD. Degenerative bone disorders such as osteoarthritis and RA commonly affect the TMJ to some degree and may cause significant disability. Refer to Figure 10.13 for an example of a malocclusion caused by rheumatoid destruction of the TMJ.

Extraoral Characteristics: The most common symptom is dull aching pain, which can radiate to the anterior neck muscles (suprahyoid and sternocleidomastoid muscles), back of the neck, and the upper shoulder muscles (Scrivani et al., 2008). The patient may also complain of frequent headaches, tinnitus, and dizziness. Chronic TMD is associated with the same type of physical, psychological, behavioral, and social issues patients with other chronic pain syndromes develop. TMD has been reported to trigger migraine headaches.

Perioral and Intraoral Characteristics: The dental hygienist may be the first professional to identify a possible TMD. A thorough history is very important and will establish the basis for determining the etiology and nature of the dysfunction. Refer to Box 10.8 for examples of questions to ask to further investigate a TMD. The most common presenting feature of TMD is pain, usually associated with muscle dysfunction; it can be localized to the tissues around the joint or it may be referred to the ear, sinuses, or head. The pain usually increases in intensity when chewing and as the day progresses into night. When pain involves the joint, it is usually confined to the ligaments and soft tissues surrounding the joint and not the bone itself. Joint dysfunction is the next most common presenting feature. Inappropriate joint sounds are the usual indicators of dysfunction. When the articular disk is out of place, the condyle will sometimes make an audible click as it bumps over it during opening and closing. Occasionally, this is very loud and sounds more like a pop. "Crepitation" is the term used for joint noise that sounds more like grinding or rubbing over a rough surface. Crepitation is felt when the articular surfaces are roughened or if the disk is damaged, allowing the bones of the joint to rub together. This type of sound is heard or felt in cases of osteoarthritis or RA. Other signs of dysfunction include deviation (the jaw moves right or left during opening or closing but returns to a normal position when fully opened or fully closed), deflection (the jaw moves to an abnormal right or left position when fully opened), limitation of opening (<40 mm between maxillary and mandibular incisors), occlusion or bite irregularities, locking in the open position, and masseter muscle hypertrophy. Many of the above signs are often seen without any accompanying pain. Panoramic radiographs are the most useful screening tool and may depict erosion of the articulating surfaces, osteophytes (bone spurs), and condylar–glenoid fossa remodeling (Scrivani et al., 2008; Guardia & Berman, 2012).

BOX 10.8 Follow-Up Questions in Reference to a Suspected TMD

- When were the symptoms first noted?
- Have they been intermittent or constant?
- What type of pain is involved? Where is the focus of the pain?
- When does the pain occur?
- Does your jaw get stuck or lock?
- Are you able to eat what you want to?
- Are you able to open your mouth as wide as you need to without pain?
- Do you have any habits such as bruxing, clenching, chewing on nonfood items, etc.?
- Do you feel stressed?
- Do you have any chronic muscle or bone disorders?
- Have you ever had treatment for TMD such as orthodontia?
- What medications are you taking?

Distinguishing Characteristics: Location and character of the pain and limitation or loss of function are characteristic of TMDs.

Significant Microscopic Findings: Not applicable

Dental Implications: Joint dysfunction can make dental/dental hygiene care difficult for the operator and very difficult and painful for the patient. The patient might be advised to take anti-inflammatory medications prior to the appointment. Appointments should be kept short, and the patient should be given frequent opportunities to close or move the mouth. Warm compresses applied to the joint in addition to the anti-inflammatory pain medications after treatment may help to alleviate posttreatment discomfort.

Differential Diagnosis: Not applicable

Treatment and Prognosis: The goal of treatment is to alleviate pain, restore function, and decrease the potential for permanent joint damage. In many cases, treatment is focused on relieving the symptoms associated with acute trauma. Nonsteroidal anti-inflammatory drugs and diet modification may be all that is necessary to allow the joint to recover from the trauma. Dietary modifications include eating softer foods, taking smaller bites, and chewing more slowly. Some patients are bothered by episodic dysfunction and pain separated by long periods of normal functioning; if the causative agent can be identified by careful history and follow-up questions, these episodes might be eliminated.

Trauma from parafunctional habits can be lessened if the patient identifies the habit and consciously tries to eliminate the behavior. Parafunctional habits such as bruxing and clenching that occur at night are more difficult to manage because the patient is not consciously aware of them. Often, soft or hard plastic occlusal night guards can help to interfere with the habit or at least decrease the trauma associated with it. Relaxation therapy and massage therapy have been used with some success in alleviating the symptoms of TMD for some individuals. In addition, ultrasonic therapy provided every other day for at least ten minutes increases the temperature of the deeper tissues, allowing for more circulation and healing. Transcutaneous electronic nerve stimulation (TENS) will relieve pain while it is being used and may relieve pain for short periods of time after use for some individuals.

Chronic trauma from altered masticatory function might necessitate making an appliance that can bring the joint and the muscles of mastication into normal resting positions, thus alleviating the constant stress on them. These appliances are usually worn at night and off and on during the day to relieve symptoms. As the symptoms resolve, the appliance is worn less often, so that the muscles are not locked into any one position for long periods of time. Dental treatment to restore posterior teeth and reestablish proper occlusion may also be necessary to restore proper function.

Most professionals who manage patients with TMD on a consistent basis recommend exhausting conservative therapy options before considering irreversible surgical procedures. Surgery may be considered in cases where the joint dysfunction is due to bony defects, growth abnormalities, and destruction or damage to the disk.

SUMMARY

- The common cold is caused by a rhinovirus or other virus. The infection causes swelling of the mucosal tissues and the production of copious amounts of mucus by the inflamed glands.
- The flu is caused by inhalation or mucosal contact with influenza virus. The flu has a short incubation period, and individuals are able to spread the virus about 2 days prior to the appearance of flu symptoms.
- Pneumonia is a lower respiratory tract infection or inflammatory reaction that can be caused by a variety of agents including viruses, bacteria, fungi, chemicals, toxic fumes, or aspirated substances such as vomitus or dental biofilm.
- Tuberculosis is caused by *M. tuberculosis,* and it is transmitted through inhalation of droplet nuclei or through contact with the mucous membranes of the respiratory tract.
- Asthma is the most serious chronic illness affecting children. Asthma results from an inflammatory reaction caused by hypersensitivity to one or more numerous triggers, such as infections, allergies, inhaled fumes, exercise, and cold temperatures.
- The most common cause of emphysema and chronic obstructive bronchitis is smoking, followed closely by inhaling secondhand smoke. Emphysema causes destruction of the lung tissue and the formation of large cavities.
- CF is the most common lethal autosomal disorder in the white population.
- GERD is a disorder of the lower esophageal sphincter that allows gastric contents to flow back up the esophagus from the stomach. Barrett esophagitis is a severe form of this damage and is associated with the potential for malignant transformation within the damaged epithelial tissues.
- Peptic ulcers are most commonly caused by an infection with *H. pylori* or by use of medications containing aspirin or other NSAIDs.
- Malabsorption syndromes are associated with an inability to absorb specific nutrients. Some of the possible oral manifestations include excessive bleeding, ulcers, glossitis, and angular cheilitis.
- Celiac disease is caused by an autoimmune reaction to gluten, which is found in wheat and many other grains. Individuals with celiac disease have difficulty maintaining proper nutrition due to malabsorption. They also often present with oral manifestations such as aphthous-like ulcers, glossitis, and enamel defects.
- Crohn disease is a granulomatous inflammatory reaction with the potential to affect any mucosal surface within the GI tract. The risk of colon cancer is increased in those with long-term disease.
- Peutz-Jeghers syndrome is an inherited disorder associated with distinctive perioral and oral pigmentations and an increased risk of cancers of the breast, pancreas, testes, ovaries, and the lining of the GI tract.
- Meningitis and encephalitis can be caused by both viral and bacterial organisms. The abrupt onset of symptoms of severe stiff neck, high fever, chills, nausea, and vomiting are characteristic of both of these infections.
- Oral manifestations of PD include dysphagia, abfraction, attrition, speech difficulties, and drooling.
- Bell palsy is unilateral paralysis of the muscles innervated by the facial nerve.
- Trigeminal neuralgia manifests as sharp intermittent pain impulses located within the tissues innervated by

the trigeminal nerve and triggered by touch, movement, or other agents.
- The most obvious clinical characteristic of BMS is the lack of any clinically observable abnormalities.
- Osteoarthritis is a multifactorial degenerative disease associated with the destruction of the articular cartilage and the bones of the joints with both genetic and environmental risk factors. RA is a chronic systemic inflammatory disorder with a multifactorial etiology associated with genetic, autoimmune, and immunological factors.
- Osteoporosis is associated with a decrease in bone density occurring primarily in women after menopause, leading to an increased risk of bone fractures, especially of the hip. Osteoporosis of the jaw can accelerate the amount of bone loss associated with a concomitant periodontal infection.
- Paget disease of bone is associated with initial bone resorption followed by enlargement of the bone with abnormal weak new bone.
- FD (monostotic and polyostotic) is caused by a gene defect that occurs after birth and is not transmissible to offspring. Cherubism follows an autosomal dominant inheritance pattern.
- The most common presenting feature of TMD is pain, which may be localized in the tissues around the joint or generalized to the surrounding areas of the skull (neck/back/shoulders). Treatment focuses on alleviating pain, restoring function, and preventing permanent joint damage.

CHAPTER REVIEW

Case Study 10.1

Your patient presents with the condition shown in Figure 10.24.

FIGURE 10.24. (Reprinted from Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999 with permission.)

1. What is the most likely cause of this type of deformity and what is it called?
2. What information should you expect to see on the patient's medical/dental history form?
3. Describe appointment modifications you may have to make for this patient.
4. Describe methods/products you might recommend for this patient to help with home care and oral disease prevention.

For answers and additional review activities, log in to **thePoint.lww.com**

Case Study 10.2

Patients who have Parkinson disease (PD) can be a challenge to manage in the dental office. You have just been informed that a 70-year-old patient with PD, Mrs. Goodhouse, has been scheduled for a dental hygiene appointment with you in 1 week. Assume that the patient has moderate symptoms that limit her ability to function independently.

1. What are the extraoral, perioral, and intraoral characteristics of this disease?
2. How can you plan for this appointment? Write a description of the modifications you might make to ensure this appointment is successful.
3. What type of home care suggestions might be appropriate for this patient? Research the Internet and other sources to find options that might be able to help this patient care for her teeth independently for as long as possible.

For answers and additional review activities, log in to **thePoint.lww.com**

Critical Thinking Activities

1. Observe the operation and physical makeup of your school's dental hygiene clinic and the public areas. What considerations have been made to try to limit the spread of colds and flu? What more could be done to limit the spread of colds and flu? Share your findings and suggestions for improvements with the rest of the class.
2. In light of research that identifies oral bacteria as playing a significant etiologic role in ventilator-associated pneumonia, what would you consider to be the role of the dental hygienist in preventing pneumonia caused by oral bacteria?

Portfolio Possibilities

- Develop an office protocol for identifying and managing a patient who has a productive cough of unknown etiology that is suspicious for TB.
- Research temporomandibular disorder (TMD) and produce a fact sheet explaining the causes and symptoms of TMD along with self-care suggestions a patient might be able to perform at home to relieve minor pain. Develop an office protocol for identifying patients with TMD.

Media Menu

Web Sites

American Dental Association—information for the professional related to treating patients taking antiresorptive medications for osteoporosis
http://www.ada.org/sections/professionalResources/pdfs/topics_ARONJ_report.pdf

Centers for Disease Control and Prevention: Tuberculosis 101—TB information for healthcare professionals
http://www.cdc.gov/tb/webcourses/TB101/default.htm

Dysphagia Resource Center
http://www.dysphagia.com/

Immunization Action Coalition—very interesting site with images and a plethora of information on vaccinations and infectious diseases
http://www.immunize.org/

Study Tools

Take advantage of additional online resources to help you study and ace your exams!

- Answers to case studies in the book
- Additional case studies and answers
- Interactive quiz bank with answer feedback
- Fully searchable e-book for quick lookup and studying on-the-go
- Expanded Media Menu with direct links to related Web sites and multimedia resources
- Supplemental references

thePoint Online resources and links are available at http://thepoint.lww.com/DeLong2e

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Chapter 10 **LESION/CONDITION SUMMARY TABLE**

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Viral cold	Rhinoviruses, coronaviruses, and others	Virus causes inflammation and swelling of the nasal passages, secretion of mucous; may contract bacterial superinfection.	Sinus congestion, runny nose, fatigue, malaise, myalgia, headache Sore scratchy throat	Not applicable	Self-limiting, resolves in 7–11 days; rest, adequate hydration; medications to reduce inflammation, secretions, and coughing	Prevent transmission with hand hygiene, cough etiquette, standard precautions; avoid direct patient care
Influenza	Influenza virus A, B, C	Short incubation period, viral shedding starts prior to symptoms and may be prolonged after the acute disease has resolved; causes necrosis of serous/ciliated cells and fluid loss into the lungs.	Symptoms include fever, headache, rapid onset of malaise; sore throat and cough	Not applicable	Antiviral medications; rest, adequate hydration, keeping warm, antipyretics for adults but avoid use in children to prevent Reye syndrome	All dental health care workers should receive an annual flu vaccination. Prevent transmission with hand hygiene, cough etiquette, standard precautions; avoid direct patient care
Pneumonia	Bacteria, viruses, toxins	Community-acquired or nosocomial, production of exudates obstructs air spaces and prevents exchange of gasses	Fever, dyspnea, productive cough, tachycardia, weakness, anorexia	Not applicable	Supportive therapy, rest, hydration, nutrition, supplemental oxygen; antibiotics or antivirals; removal of offending chemical agent	Oral bacteria in dental biofilm can be aspirated by a susceptible individual; adequate oral care performed daily by hospital personnel or others reduces incidence.
Tuberculosis (TB)	*Mycobacterium tuberculosis* multidrug-resistant (MDR), extensively drug-resistant (XDR)	Initial infection contained by the immune system in tubercle (LTBI); reactivation or reinfection causes formation of many tubercles, leading to atelectasis and hemoptysis, and destruction of the lungs.	LTBI is asymptomatic; TB disease—afternoon fevers, weight loss, night sweats, weakness, chest pain, productive cough, and hemoptysis	Presence of acid-fast bacilli (AFB)	Treatment mainstays are isoniazid and rifampin for 3–9 months; new treatment regimen consists of 12 once-a-week doses for 12 weeks.	Identify suspected cases of undiagnosed TB and refer, delay treatment until considered noninfectious; if necessary, use a personal respirator effective at the N-95 particulate level
Asthma	Unknown, related to various triggers	Triggers elicit an inflammatory response, which causes smooth muscle spasm, edema, production of thick mucus; respiratory obstruction and inability to completely empty the lungs.	Spasms of wheezing, cough and dyspnea; continuous attacks termed status asthmaticus are considered life threatening. Medications increase the risk of fungal infections, cause xerostomia, GERD, and erosion.	Not applicable	Bronchodilators, anti-inflammatories, and corticosteroids are the mainstay of treatment.	Educate patient on how to manage side effects of drugs, avoid triggering events during dental treatment (limit aerosol production, avoid latex); keep the patient's inhaler out and reachable in case of emergency, avoid prescribing or recommending medications that contain aspirin; educate about caries prevention and salivary stimulation.
Chronic obstructive pulmonary disease (COPD)	Tobacco smoking and inhaling secondhand smoke; air pollution, occupational exposure to toxins, heredity	Emphysema: decreased elasticity of lungs Chronic obstructive bronchitis: obstruction of the small airways by inflamed, hyperplastic mucosal tissues	Emphysema: Pink puffers, increase rate of breathing, barrel chest, weight loss Chronic obstructive bronchitis: Blue bloaters, airways blocked, cannot maintain sufficient oxygen in tissues.	Not applicable	Treatments improve quality of life: bronchodilators, anti-inflammatories, expectorants.	Patient positioning to ease breathing, supplemental oxygen, avoid creating aerosols, tobacco cessation; medications may produce xerostomia, education about caries prevention, salivary stimulation.

Chapter 10 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Cystic fibrosis (CF)	Mutation of CFTR gene on chromosome 7 Autosomal recessive	Defective cells lining the respiratory system, pancreatic ducts, bile ducts, sweat glands, and salivary ducts produce abnormally thick secretions that obstruct the ducts.	Chronic coughing and wheezing, chronic lung infections, underweight, malnourished, barrel chest, clubbing of fingers Xerostomia, high caries risk, increased risk of fungal infections	Not applicable	Focused on preventing lung infections, promoting nutrition, and alleviating symptoms associated with abnormal mucus	Consult with physician about prophylactic antibiotics, vitamin K supplements; minimize exposure to aerosols, position to promote easy breathing and mucus drainage; avoid the use of nitrous oxide; education about caries prevention, salivary stimulation is essential.
Dysphagia	Various physical, neoplastic, and neurological entities	Varies depending on etiology	Aspiration pneumonia, regurgitation of food, and malnutrition Foul odor caused by food trapped and fermenting in a diverticula pouch	Not applicable	Physical therapy to train musculature, small meals, thickened liquids, other treatments according to etiology	Position the patient to prevent accidental aspiration of fluids and debris during dental care
Gastrointestinal (GI) reflux disease	Weak lower esophageal sphincter muscle	Exposure to gastric acids causes erosions in mucous membranes; Barrett esophagus is associated with an increased risk of adenocarcinoma.	Heartburn, belching, wheezing, coughing, hoarseness, pain centered in the chest, throat, shoulders and back Increased risk for enamel erosion and pharyngeal cancers	Not applicable	Medication to reduce acid, smoking cessation, avoidance of foods associated with decreasing effectiveness of sphincter muscles	Patient positioning to lessen GERD symptoms, fluoride applications with custom trays, routine fluoride varnish every 3 months, educate about destruction caused by toothbrushing at the wrong times; restore damaged teeth; educate about caries prevention
Peptic ulcer	Infection with *Helicobacter pylori (H. pylori)* Aspirin or nonsteroidal anti-inflammatory drugs (NSAIDs)	Mucosal inflammation weakens the surface tissues and increases risk of injury, compromised surface mucosa comes in contact with gastric acid, causing ulceration, bleeding, and often perforation	Pain relieved by eating, anorexia, weight loss, bleeding, malnutrition Enamel erosion	Not applicable	Eliminate infection with antibiotic therapy, reduce production of acid; avoid the use of medications containing aspirin or NSAIDs	Food choices and frequent eating may encourage caries; vomiting will increase acid erosion. Education about caries prevention is essential.
Celiac disease	Complex genetic basis	Glutton triggers an autoimmune reaction that destroys the intestinal villi, resulting in inability to absorb adequate nutrients.	GI symptoms associated with inability to absorb fats, anemia associated with malnutrition, bleeding, osteoporosis Oral ulcers, glossitis, enamel defects; increased risk of cancer (oropharynx, esophagus, pancreas)	Not applicable	Total elimination of glutton from the diet, possible use of corticosteroids	Identify oral ulcers and enamel defects as possible indicators of celiac disease, correlate with other associated GI symptoms and refer for a medical evaluation

continues

Chapter 10 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Crohn disease	Multifactorial genetic and environmental and host factors	Chronic granulomatous inflammatory reaction resulting in ulcerations involving all layers of the GI tissues, may become deep fissures and communicate with other parts of GI tract or skin; scarring causes difficult absorption of nutrients.	Diarrhea, abdominal pain, nutrient deficiencies, weight loss, growth retardation in children, GI tract bleeding Multiple aphthous-like ulcers, swelling of the mucosa, angular cheilitis, glossitis, cobblestoning	Not applicable	Medications: anti-inflammatories, immunosuppressants, antidiarrheals or laxatives TNF–blocking drugs; nutritional supplements Surgical removal of the affected area may be necessary. Topical steroids to control oral ulcers	Nutritional counseling to help avoid oral manifestations due to malnutrition; do not prescribe or recommend pain medications containing aspirin or NSAIDs
Peutz-Jeghers syndrome	Mutation of *STK11/LKB1* tumor suppressor gene on chromosome 19 Autosomal dominant	Genetic mutation causes development of intestinal polyps that may become malignant and a higher risk for cancer of the breast, lung, pancreas, gonads, and thyroid	Brown or dark blue cutaneous macules concentrated on face, hands, fingers, feet, and toes; intestinal polyps (may become malignant) and higher risk of other cancers Perioral and muscosal brown or dark blue macules	Not applicable	Identification of the syndrome with lifetime monitoring for early intervention of malignancies	Identify the characteristic perioral pigmentation and refer for medical evaluation if appropriate
Meningitis and encephalitis	Bacterial and viral organisms	Meningitis affects all layers of the covering of the brain; encephalitis causes generalized edema, hemorrhage, and necrosis of brain and spinal tissues.	Headache, stiff neck, fever, chills, vomiting, altered mental status Meningitis may present with abrupt symptoms resulting in death within 24 hours	Not applicable	Antibiotics for bacterial infections, corticosteroids to reduce inflammatory response	Education about CDC recommendation for vaccination 9 preadolescents, teenagers, college-bound students) Identify signs and symptoms to make a timely referral
Parkinson disease (PD)	Unknown; genetic, environmental, and viral agents are possible.	Destruction of cells in the substantia nigra that produce dopamine results in movement and balance dysfunction.	Tremors, rigidity, drooling, akinesia; depression, dementia Masklike facial expression, parafunctional movements increase attrition and abfraction, dysphagia, dysarthria.	Degeneration of neurons in the substantia nigra	Medications to control the symptoms and possible deep brain stimulation; there is no cure at the present time.	Modify treatment to accommodate for uncontrolled movements, take precautions to avoid injuries (bite blocks/mouth props); educate about xerostomia, side effects of medications, caries prevention, and salivary stimulation; more frequent, short maintenance appointments; modify home care techniques and implements to increase ability to perform self-care
Bell palsy (facial nerve paralysis)	Unknown, various agents suspected	Paralysis may be the result of pressure on the nerve and loss of the myelin sheath from edema.	Unilateral paralysis of facial muscles, dry eyes, pain, numbness, hyperacusis Drooling, slurred speech, dysphagia, loss of gag reflex, diminished salivary flow, dysgeusia	Not applicable	Most recover without treatment, corticosteroids have been used to offer the best chance for a full recovery; surgical treatment restoring some function to the facial muscles is successful in some unresolved cases.	Safety precautions related to eye protection during treatment and avoiding self-inflicted injury due to local anesthetics; educate about food accumulation or "pocketing," dysphagia, xerostomia, caries prevention, and salivary stimulation; frequent maintenance appointments

Chapter 10 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Trigeminal neuralgia	Unknown or sometimes associated with vascular or neoplastic factors	Damage to the small and large nerve fibers causes chronic severe pain.	Major manifestation is severe incapacitating pain triggered by touch or other stimuli not usually considered painful; triggering can occur on the skin or the oral mucosal surfaces.	Not applicable	Focuses on preventing pain; medications include anticonvulsants, antidepressants, BOTOX surgical destruction of parts of the nerve	Patients may avoid all self-care procedures for fear of triggering a painful episode; refer to professionals who can help with a chronic pain disorder.
Migraine headache	Complex interaction of vascular and neural factors	One theory states neurons of the cerebral cortex become hyperexcited leading to a change in blood flow to the brain.	May have a preceding "aura" followed by severe unilateral pain, throbbing, nausea, vomiting, photophobia, noise sensitivity Oral signs may include numbness of the face, tongue, and lips and speech or language dysfunction.	Not applicable	Medications to address pain and other symptoms, prophylactic medications to prevent headaches, alternative therapies	Most medications cause xerostomia; education about caries prevention and salivary stimulation is essential.
Burning mouth syndrome (BMS)	Idiopathic	Unknown, but many feel it is a neuropathy that results in chronic pain.	Burning pain in the oral soft tissues (tongue, hard palate, and lower lip most often) with no clinical evidence of pathology; symptoms become more severe as the day progresses, usually no symptoms during sleep, xerostomia and taste perversions.	Not applicable	Identify cause and treat; if cause is unknown may try medical treatment with clonazepam or paroxetine; patient should avoid mouth rinses containing alcohol or strong flavoring, refrain from tobacco use	Reassure the patient, rule out other dental etiologies, refer for medical evaluation, education about caries prevention and salivary stimulation if appropriate
Osteoarthritis	Multifactorial degenerative disease	Cartilage covering articular surfaces in synovial joints is progressively destroyed resulting in bone-on-bone contact, debris in the joint space, and formation of osteophytes, resulting in limitation of motion and pain	Pain in the weight-bearing joints, joints of the hands, and cervical and lumbar spine; Heberden nodes TMJ involvement is common; crepitus, deviation, deflection, and limited movement.	Not applicable	Treatment focuses on relieving pain and prolonging function of the joints, anti-inflammatory drugs, arthroscopic surgery to remove free floating debris, total joint replacement	Position patient for comfort, short appointments, recommend home care modifications for effective control of biofilm, plan to control bleeding due to anticoagulant effect of most NSAIDs
Rheumatoid arthritis (RA)	Strong genetic risk and other factors	Autoimmune inflammatory reaction involving joints and other organs, results in fusion of the joints, deformity and loss of function	Pain, morning stiffness, soft tissue swelling, and accumulation of fluid around joints, rheumatoid nodules, carpel tunnel syndrome, dry eyes, fluid accumulation around the heart and lungs Destruction of the TMJ is common.	Not applicable	Focused on slowing disease progression, preventing deformities, eliminating pain; DMARDs are the mainstay of therapy; anti-inflammatories help to control pain; exercise and rest are also important.	Pay attention to medications: immunosuppressants (decreased immune function) and corticosteroids (decreased bone density); determine INR prior to care if appropriate; position patient for comfort, educate about caries, periodontal disease, and salivary stimulation

continues

Chapter 10 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Osteoporosis	Unknown, associated with endocrine disorder or corticosteroid medications	Defective bone remodeling causes a decrease in the density of the bone, leading to pathological fractures.	Decrease in height, dowager's hump, lower back pain, fractures Thinning of the maxilla and mandible, more rapid periodontal bone loss Possible ARONJ	Low mineral density	Focus of therapy is to maintain or increase bone density with medications, exercise, and adequate ingestion of calcium and vitamin D	Identify patients taking antiresorptive medications, monitor for signs of ARONJ, educate about increased risk for ARONJ after invasive dental procedures, advise patient to look for signs of ARONJ; discuss osteoporosis prevention with all female patients
Paget disease	Unknown	Resorption of cancellous bone that is replaced with a vascular connective tissue and then rapid creation of abnormal bone that causes enlargement of the affected structures	Spinal involvement causes neurologic symptoms, paralysism significant increase in alkaline phosphatase, asymmetric enlargement of skull and facial bones, nerve compression, enlargement of the jaws,TMD, loss of lamina dura and PDL space, hypercementosis	Enlargement and "cotton-wool" appearance of affected bones on radiographs	Disease is often self-limiting and requires no treatment; otherwise, medical treatment depends on the severity of symptoms; antiresorptive drugs are usually used to slow bone growth and resorption.	Manage oral problems associated with enlarging jaw bones, malocclusion, TMJ dysfunction, pain management due to compressed nerves, advise patients taking antiresorptive drugs about ARONJ and educate about signs and prevention
Fibrous dysplasia (FD)	FD: defective gene Cherubism: autosomal dominant	Spongy/cancellous bone is replaced by fibrous tissue, which is then replaced by an immature "woven" bone.	Monostotic: affects one bone, often the maxilla or mandible Polyostotic: affects more than one bone McCune-Albright syndrome: polyostotic plus café au lait macules and endocrine disorder/s Jaffe-Lichtenstein syndrome: polyostotic plus café au lait macules without endocrine disorders Cherubism: affects bones of face causing enlargement of cheeks, upward tilt of eyes and other dental abnormalities	Radiographic "ground-glass" appearance of the bone and multilocular cystic appearance of the jaw bones in cherubism	Treatment may be unnecessary for small mono- or polyostotic lesions; otherwise, surgical remodeling is often necessary.	Children with cherubism require extensive dental care starting at diagnosis of the disorder and continuing for life.
Temporomandibular disorder (TMD)	Trauma, degenerative diseases	Acute trauma: cardinal signs of inflammation Chronic trauma: more gradual course; chronic pain and loss of function Growth disorders: may present as an asymmetrical enlargement Degenerative diseases: progressive loss of function and pain.	Pain that may radiate to surrounding structures; headache; tinnitus; and dizziness. Pain increases with function, abnormal sounds (crepitus or clicking/popping), deviations or deflections, limitations in opening, locking in the open or closed position, masseter muscle hypertrophy.	Panoramic radiographs may show erosion of articular surface, joint remodeling, or bone spurs.	Treatment depends on severity of symptoms, anti-inflammatory drugs, diet modification, night splints, relaxation and massage therapy, construction of an appliance to move jaw into proper position and take stress off of the TMJ, surgery as a last resort to treat severe TMD not alleviated by other treatments	Identify patients with TMD and discuss methods to reduce pain and increase function, modify treatment by using bite blocks or mouth props and providing opportunities to close or move the mouth often, recommend anti-inflammatory medications before and after treatment

PART II

Oral Pathology

CHAPTER 11 **Lesions That Have a Vesicular Appearance**
Nancy W. Burkhart

CHAPTER 12 **Ulcers and Ulcer-Like Lesions**
Nancy W. Burkhart

CHAPTER 13 **Lesions in Shades of Red and Purple**
Nancy W. Burkhart

CHAPTER 14 **White Lesions**
John M. Wright

CHAPTER 15 **Pigmented Lesions**
Nancy W. Burkhart

CHAPTER 16 **Raised Lesions with a Rough or Papillary Surface**
Valerie Murrah

CHAPTER 17 **Soft Tissue Enlargements**
Valerie Murrah, Nancy W. Burkhart

CHAPTER 18 **Hard Tissue Enlargements**
Nancy W. Burkhart

CHAPTER 19 **Radiopaque Lesions**
Nancy W. Burkhart

CHAPTER 20 **Radiolucent Lesions**
Nancy W. Burkhart

CHAPTER 21 **Abnormalities of the Teeth**
Harvey P. Kessler

CHAPTER 22 **HIV and AIDS**
Jacqueline M. Plemons

CHAPTER 23 **Skin Lesions**
Nancy W. Burkhart

CHAPTER 11

Lesions That Have a Vesicular Appearance

KEY TERMS

Acantholysis	Necrosis
Ankyloglossia	Nikolsky sign
Antipruritic	Noncytotoxic virus
Autoinoculation	Pathognomonic
Bulla	Pemphigus vulgaris
Corticosteroids	Perioral skin
Cytotoxic viruses	Postherpetic neuralgia (PHN)
Desquamative gingivitis	Primary herpetic gingivostomatitis
Dysphagia	Prodromal
Erythema	Pruritus
Forchheimer sign	Ramsay Hunt syndrome
Hand-foot-and-mouth disease	Ranula
Herpangina	Rubella
Herpes labialis	Rubeolla
Herpesviridae	Sialolith
Herpes zoster	Subclinical infections
Herpetic whitlow	Symblepharon
Immunosuppression	Tzanck cells
Koplik spots	Ulceration
Lymphadenopathy	Varicella
Microstomia	Vesicular lesions
Mucocele	
Mucus extravasation phenomenon	
Mucus retention cyst	

LEARNING OUTCOMES

1. Define the key terms used in this chapter.
2. Describe the clinical features of the mucocele.
3. State the difference between a mucocele and a mucus retention cyst.
4. State four of the trigger mechanisms that are involved with herpes simplex virus (HSV) infections.
5. List the sites that may be affected by the HSV infections.
6. List at least three sites where a person may self-inoculate with HSV.
7. Describe the cycle of varicella–zoster virus infection and the subsequent reactivation resulting in shingles along with postherpetic neuralgia (PHN).
8. List the organisms involved in hand-foot-and-mouth disease, rubeola, rubella, herpes labialis, and herpangina.
9. Name four major types of pemphigus vulgaris.
10. Describe the histologic findings that would differentiate pemphigus vulgaris from mucous membrane pemphigoid.
11. Describe the key factors of the immunofluorescence diagnostic test in the differentiation of pemphigus vulgaris and pemphigoid.
12. List the four major categories of epidermolysis bullosa (EB) from less severe to most severe.
13. List three diseases to consider in a clinical differential diagnosis involving pemphigoid.
14. Discuss the importance of requesting a thorough eye examination when a diagnosis of mucous membrane pemphigoid or pemphigus vulgaris has been made.
15. Discuss the definition of cytotoxic and noncytotoxic.
16. Discuss the etiology of EB acquisita.
17. Describe the clinical manifestations of EB.
18. List the areas of the body that are most often affected by the dystrophic form of EB.

CHAPTER OUTLINE

Traumatic or Inflammatory Lesions
- Mucocele

Infectious Viral Diseases
- Herpes Simplex Virus (HSV)
  - Human Herpesvirus Type 1
    - Primary herpetic gingivostomatitis
    - Secondary or recurrent herpes simplex infections
  - Other Forms of Herpes Simplex Infection
    - Herpetic Whitlow
    - Ocular Herpes
    - Herpes Simplex Virus and Genital Herpes
    - Primary varicella–zoster (chickenpox)
    - Secondary varicella–zoster (shingles or herpes zoster)
- Coxsackievirus Infections
  - Hand-foot-and-mouth disease
  - Herpangina
  - Acute Lymphonodular Pharyngitis
- Paramyxoviridae Virus Infections
  - Rubeola (measles)
- Togavirus Infections
  - Rubella (German measles)

Noninfectious Vesiculobullous Diseases: Autoimmune Diseases
- Pemphigus vulgaris
- Pemphigoid
  - Mucous membrane pemphigoid (cicatricial pemphigoid, benign mucous membrane pemphigoid)
  - Bullous pemphigoid

Congenital or Genetic Diseases
- Epidermolysis bullosa
- Epidermolysis Bullosa Acquisita

RELATED CLINICAL PROTOCOLS

#1 Performing a Cytology Smear
#2 Applying Topical Corticosteroids in the Mouth
#3 Maintenance Appointment Guidelines for the Patient with a Mucosal Disease
#7 Patient Education: Recommendations for Recurrent Herpes Labialis
#8 Treating Patients with Intraoral Ulcers (Recurrent Aphthous Ulcers, Traumatic Ulcers, or Recurrent Intraoral Herpes)
#24 Tobacco Cessation

Vesiculobullous disorders are sometimes grouped as similar in appearance when seen by the clinician. However, with careful evaluation clinically and with the help of diagnostic tests, these lesions can usually be differentiated quite successfully. Based on the patient history, the clinical appearance, and some investigation, the astute clinician can combine the clues observed to solve the mystery. This chapter addresses those lesions in the mouth that have a vesicular appearance. They may be categorized as traumatic or inflammatory lesions, lesions from known infectious agents, immune system disorders, or those that have a genetic or congenital component.

Traumatic or Inflammatory Lesions

Traumatic lesions with a vesicle-like appearance may sometimes be ulcerative, or they may have a smooth tissue appearance with only slight color differentiation. The lesion may be benign, or some may be more serious and need further evaluation to confirm a diagnosis. A careful evaluation will usually provide the clinician with enough information to sort out the etiology and the course of action related to the lesion.

NAME: Mucocele

The **mucocele** is a painless, benign, dome-shaped, soft, fluctuant nodule that has prevalence for the inside of the lower lip. The mucocele may be a single nodule, or there could be multiple nodules involved in a single area of the mouth. The mucocele is also known as the mucus extravasation phenomenon (lined with granulation tissue and filled with mucus), mucous cyst, and mucous retention cyst (when lined with epithelium). The most preferred term is **mucus extravasation phenomenon**. This entity is one of the most common oral findings and may have diverse clinical appearances. Figure 11.1A depicts a mucocele in the buccal mucosa. Figure 11.1B depicts the histology of a mucocele. The accepted term is "mucus extravasation phenomenon," or sometimes you will also see "mucous retention cyst"—however, most pathologists prefer that the term cyst be reserved for those lesions that exhibit an epithelial lining. In addition to not having an epithelial lining, mucoceles are caused by a ruptured duct expelling fluid where a cyst actually retains the fluid within (Damm, 2010). Similarly, **ranula** occurs in the floor of the mouth affecting the ducts of the sublingual and submandibular glands. The ranulas can be very large and are covered in more detail in Chapter 17. The lower lip appears to be a prime location for the occurrence of the mucocele. However, mucoceles may occur in other locations with less frequency such as the ventral tongue, the hard and soft palate, buccal mucosa, retromolar area, upper lip, and the lingual frenum (Chi et al., 2011).

Etiology: Mucoceles are caused by trauma and severance of an accessory salivary excretory duct. The damage to the ductal structure causes mucin to be retained in the surrounding tissue. The lesions related to the mucocele are discussed in more detail in Chapter 17 under salivary gland disorders. The mucocele is mentioned here because the lesion, depending upon the location and whether it is more superficial, may appear vesicle-like. The mucous retention cyst results from a sialolith, or salivary gland stone, and sometimes from ductal scar tissue, causing obstruction of

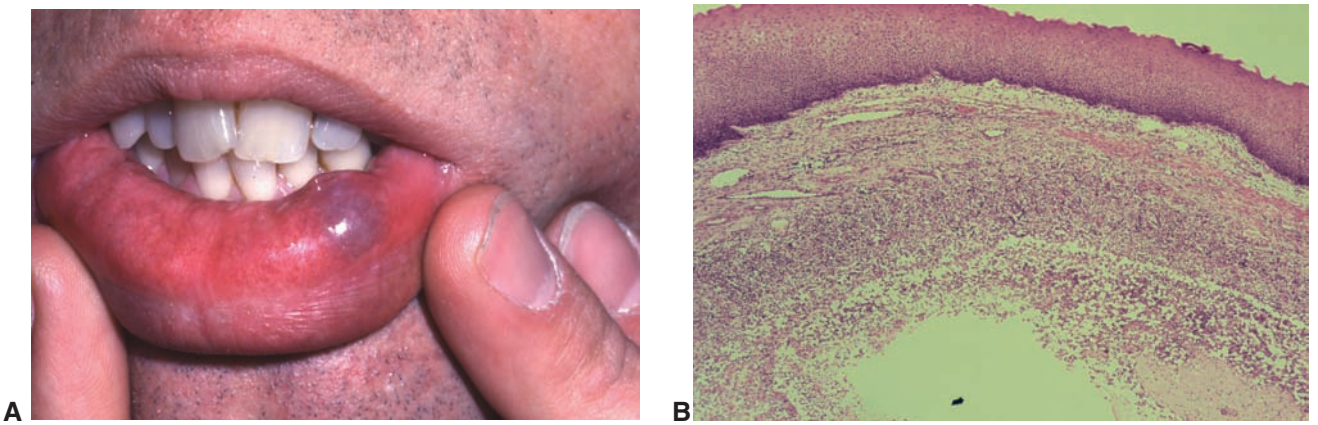

FIGURE 11.1. A. A mucocele in the buccal mucosa region. (Courtesy of Dr. Harvey Kessler.) **B.** Histology of a mucocele.

the involved salivary gland. As stated previously, the fluids are retained within the structure of the cyst. Usually found in older adults, the mucous retention cyst is often found in the floor of the mouth. Figure 11.2 shows a mucous retention cyst in the floor of the mouth.

Method of Transmission: There is no method of transmission of the mucocele because the lesion is caused by trauma.

Epidemiology: The younger age groups are most often affected, because of the traumatic nature of the lesion. Both sexes are affected equally in most literature. Recent studies by Jani et al. (2010) report a male prevalence of 36 patients with a male-to-female ratio of 1.77:1 and a vast age range of 6 years to 66 years in age with a mean age of 23.55. Studies by Chi et al. (2011) reported no significant gender predilection in a much larger population of 1,715 confirmed oral mucoceles but also reported a similar age range of 24.9 years. Other studies by Hayashida et al. (2010) in a group of 173 patients report a female predilection with most patients in the second decade of life. Seventy-eight percent of these patients reported previous trauma, and the site was the lower lip area.

Pathogenesis: The mucocele occurs when a salivary gland duct is severed through trauma and the contents of the duct collect in the tissue, manifested with a raised, seemingly fluid-filled lesion often exhibiting a soft blue hue. The more superficial mucoceles will rupture spontaneously, leaving an ulcer-like lesion.

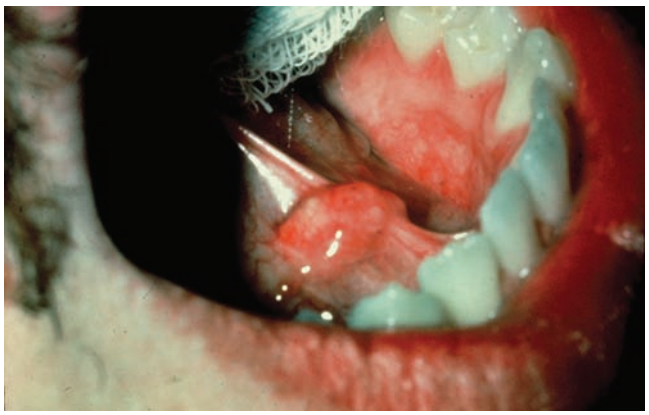

FIGURE 11.2. Mucous retention cyst in the floor of the mouth. (Courtesy of Dr. Carolyn Bentley.)

Extraoral Characteristics: None

Perioral and Intraoral Characteristics: Mucoceles may have a blue hue with a somewhat transparent appearance that can vary depending upon their proximity to the surface epithelium. Most appear slightly elevated and exhibit a smooth appearance. This is especially true when they occur in the oral mucosa of the lip area. Mucoceles may also appear in the palate, and they may be in any area where there is salivary gland function or accessory gland ducts. Mucoceles are asymptomatic in almost all cases. The size may vary greatly, ranging from a few millimeters to centimeters, and is usually under 1.5 cm.

Distinguishing Characteristics: The cloudy blue hue of the mucocele is a distinguishing characteristic and is often used in clinical differentiation of the lesion. The color variation depends upon how close to the surface the mucin may pool. The patient may be able to confirm that the lesion increases and subsequently decreases in size after trauma because of a rupture in the lesion. Reports of the size vary from millimeters to centimeters. Chi et al. (2011) cautioned that there are variants that should be considered in a diagnosis. These occur infrequently, but recognition of the fact avoids misdiagnosis.

Significant Microscopic Features: The mucocele is walled off by granulation tissue enclosing the mucin pool. The severed duct shows ductal dilation, and an inflammatory response is initiated. Mucoceles are not true cysts, since they are not epithelial lined. Mucous retention cysts or mucous cysts result because of a salivary gland stone or sialolith composed of calcium carbonate. Additionally, epithelial tissue lining the cyst should be observed microscopically in order for this diagnosis to occur.

Dental Implications: The main dental implication would be tissue trauma to the buccal mucosa or the lip region

because of the elevated tissue and tendency for the patient to traumatize the area while eating or chewing. Recent studies by Syebele and Butow (2010) report an increase of both mucoceles and ranulas in patients with HIV infection. In their study, 68.75% of a small group of patients tested positive for HIV after entering a facility with a chief complaint of a mucocele or ranula. Since the study was in South Africa with high rates of HIV infection, the implications of the findings are not conclusive or generalizable to other groups. Other studies have reported increased rates of HIV infection with ranulas (see Chapters 17 and 22). This may be a consideration when discovering such lesions and may warrant further questioning.

Differential Diagnosis: Considerations may be neoplasms, lipomas, vascular malformations, a dermoid cyst (when in the floor of the mouth), as well as mucoepidermoid carcinoma in the palate region. Sometimes, the clinical and microscopic features may be mistaken for other conditions such as pemphigoid, bullous lichen planus, papilloma, fibroma, or recurrent HSV infections.

Treatment and Prognosis: When a mucocele is classified as a mucous cyst or blockage of the duct, surgical approaches are warranted. These approaches are discussed in Chapter 17 under salivary gland diseases and may include surgery with marsupialization and laser ablation.

Infectious Viral Diseases

Viruses may be **cytotoxic** or **noncytotoxic.** Cytotoxic viruses replicate within the host cells and destroy them, releasing new viral particles into adjacent tissues. These particles go on to invade other host cells, allowing progressive cellular destruction to take place. As more host cells are destroyed, more symptoms develop. Humans are exposed to viruses daily, but no symptoms occur if the immune system is healthy. If the body's defenses become weakened, however, through fatigue, stress, injury, or other factors, the person is more susceptible to the cellular destruction.

Noncytotoxic viruses do not cause cellular destruction or they may cause it on an intermittent basis. The virus may lie dormant in an infected cell or take the place of some of the host DNA and become part of the cell. For example, herpesvirus may remain dormant for long periods but become activated when host defenses are altered.

Differentiation between viral and nonviral diseases is important in determining the treatment for a particular lesion. If the disease is viral, the treatment should be started no later than 48 hours after the onset of symptoms to achieve optimal success. If cell destruction and viral replication have occurred before the clinician views the oral lesions, the antiviral medications may be less effective. Antiviral medications are most effective in the **prodromal** stage, when the individual experiences localized tingling, burning, or **pruritic** sensations (pruritus) that signify a pending viral outbreak. The following viral infections are the most common.

Herpes Simplex Virus

Herpes simplex virus (HSV) is a member of the human herpesvirus (HHV) family known as **Herpesviridae**. At least eight HHVs have been identified, including those involved in AIDS-related illnesses. HHV-1 and HHV-2, however, are the most common. The virus may be in either a primary form or a recurrent form. HHV-1 is associated with primary herpetic gingivostomatitis, recurrent oral herpes, and herpes labialis; type 2 (HHV-2) is associated with genital herpes. However, it is known that type 2 may be found orally because of oral–genital contact (Lamey et al., 1999), and likewise, HHV-1 may cause genital lesions.

The two are structurally similar, and their manifestation is identical, but they are antigenically different. In other words, the immune system recognizes them as two distinct entities. There may be some protection from antibodies that cross over (antibodies to HHV-1 may reduce the severity of the response to HHV-2). In this book, the discussion focuses on the orofacial infection of type I HHV that will be called herpes simplex or "HSV" throughout the chapter. Additionally, in the same family of the Herpesviridae, included are the varicella–zoster virus (VZV), Epstein-Barr virus, cytomegalovirus, roseola (HHV-6 and HHV-7), and Kaposi sarcoma virus. Other viruses that can cause orofacial involvement include rubeola (measles or Paramyxovirus), rubella (German measles or togavirus), herpangina, and hand-foot-and-mouth disease (both coxsackieviruses).

Human Herpesvirus Type 1

As mentioned above, HHV-1 (HSV) is commonly associated with the oral conditions that are described in the following sections.

NAME: Primary herpetic gingivostomatitis

Etiology: The virus is commonly encountered and acquired during childhood. **Primary herpetic gingivostomatitis** is caused by HHV-1 (HSV). Figure 11.3A demonstrates a primary herpetic infection with vesicles on the lip, tongue, and buccal mucosa.

Method of Transmission: Transmission occurs through close physical contact such as kissing, shared utensils, aerosols (such as sneezing or coughing), and close, crowded living conditions. The virus is more readily transmitted in dense and crowded populations of the world. Typically, the virus is spread through saliva and has a propensity toward the pharynx, eyes, lips, and oral areas. The virus can also be transmitted when there are no symptoms or lesions, as the infected person sheds virus particles in early stages. Mucosa and nonintact skin are susceptible to infection. (See Clinical Protocol #8 for the treatment of herpes and intraoral ulcers.)

Epidemiology: Exposure of one-half of the U.S. population and even up to 85% of populations in crowded living areas

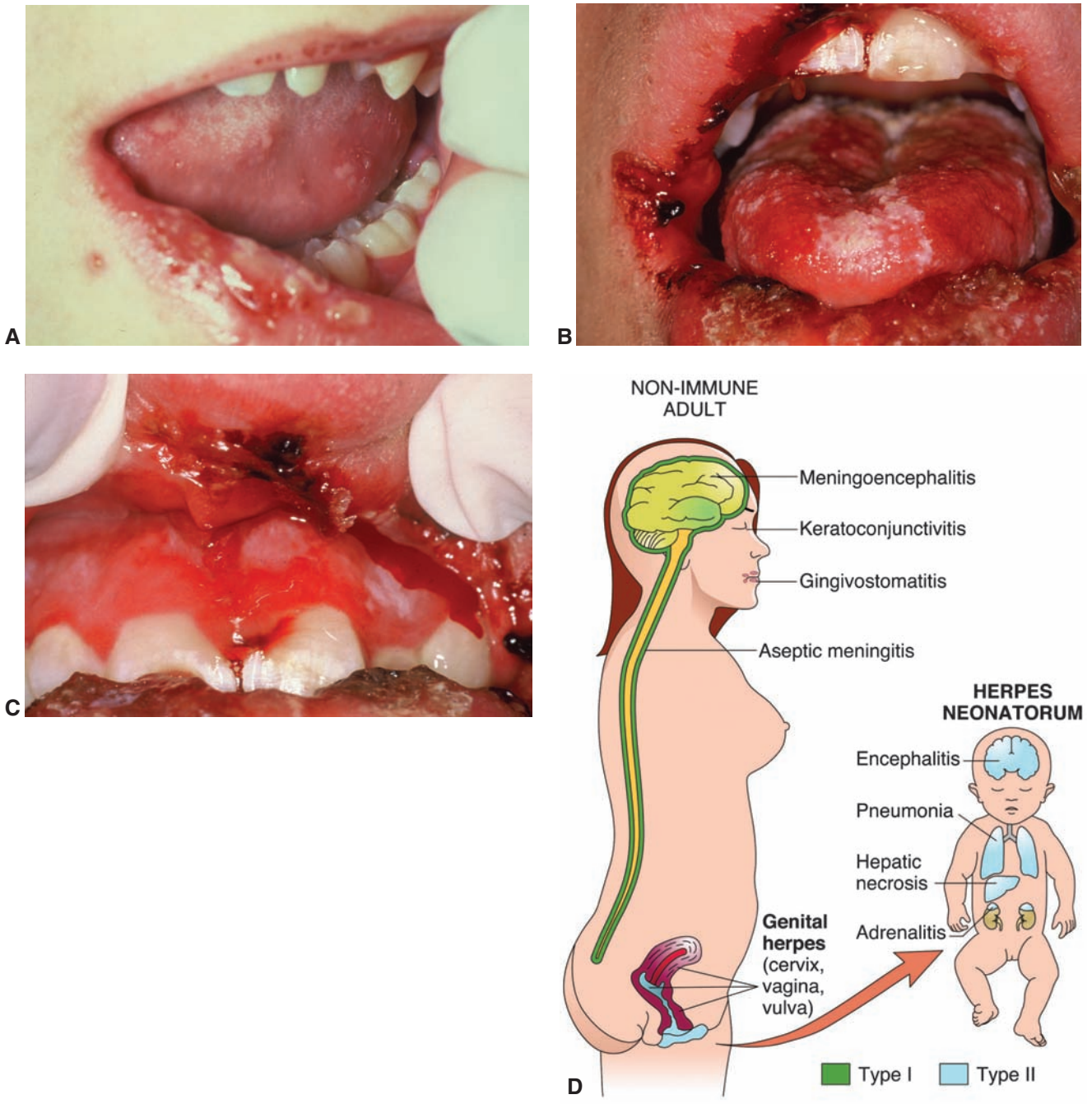

FIGURE 11.3. **A.** Primary herpetic gingivostomatitis; lip lesions and tongue lesions. (Courtesy of Dr. Michael Brennan.) **B.** Primary herpetic lesions. (Courtesy of Dr. Terry Rees.) **C.** Primary herpetic lesions. (Courtesy of Dr. T.D.Rees.) **D.** Cycle of herpes infections. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott William & Wilkins, 1999.)

has been found. The infection shows no sex predilection. Additionally, those populations who were never exposed to the virus at a young age are most commonly affected. Children usually exhibit a subclinical infection and may never know that they have been infected.

Pathogenesis: The initial exposure of an individual to the virus is called the primary infection. Recurrent episodes are termed secondary forms. More than 85% of adults in both urban and rural areas have antibodies, showing that they have been exposed to the HSV. Usually, individuals develop antibodies to herpesvirus during childhood at between 6 months and 6 years of age. Many of these individuals are not aware of ever experiencing the primary infection, while others remember being quite ill. After mucocutaneous contact with an infected individual, there is a 2-day to 2-week incubation period with fever and lymphadenopathy. The disease may present as either a subclinical or a clinical infection, but most primary infections are subclinical. Usually, individuals develop antibodies to herpesvirus

during childhood at between 6 months and 6 years of age. However, the primary infection may occur in adulthood in those individuals who were not exposed to the virus as children. Following resolution of the primary infection, antiherpetic antibodies are formed, although the antibodies may not be effective in eliminating the herpes virus. For a small percentage of patients, the virus may migrate along the trigeminal nerve to the trigeminal ganglion, where it will remain latent until triggered by some future event.

Extraoral Characteristics: HSV may be found in the oral or genital areas. When found in the genital area, herpes simplex presents as multiple, painful ulcerations on any mucosal or cutaneous surface. The two are clinically indistinguishable regardless of lesion site.

Perioral and Intraoral Characteristics: The classic feature of this condition is a fiery red, marginal gingivitis that usually affects all areas of the dental arches as shown in the primary severe herpetic lesions in Figure 11.3A–C.

Multiple, small vesicular lesions appear on the gingiva, lips, tongue, oral mucosa, and occasionally on perioral skin. The vesicles rupture quickly and appear as ulcerations surrounded by erythema.

Distinguishing Characteristics: The individual experiences extreme pain, elevated temperature, and generalized malaise. Cervical lymphadenopathy and a sore throat commonly occur. Signs and symptoms may be more severe when it occurs in adults. The cycle of primary HSV exposure is represented in Figure 11.3D.

Significant Microscopic Features: HSV exhibits intraepithelial vesicle formation. The clinical characteristics of the disease are readily apparent to the clinician in most cases, but other tests can provide a definitive diagnosis when necessary. The cells of HSV are readily apparent in most cases when viewed microscopically. The cells that are infected with HSV appear as virus-infected epithelial cells with inflammatory cells and a ballooned, degenerating appearance with microscopic inclusions and multinucleation. Figure 11.4 shows the histology of a HSV-infected cell.

A biopsy, cytologic smear, or viral culture can provide a definitive diagnosis when necessary.

Dental Implications: The clinical appearance and course of the infection are significant factors in determining this diagnosis. Beginning or completing dental treatment on a patient with herpetic lesions is detrimental because of the risk of spreading the virus. Treatment should be rescheduled until the lesions have healed. Eating is the most significant problem because the course of the disease is usually 10 to 14 days. Patients should be encouraged to keep hydrated.

Differential Diagnosis: Diagnosis is based on clinical presentation. Differentiation must be made with other vesicles that occur orally such as the following:

1. *Recurrent aphthae*—Elevated temperature may or may not be present with the ulcers, and they usually appear as single lesions rather than coalescing groups. Aphthae appear on freely moveable nonkeratinized mucous membranes such as the labial mucosa, maxillary and mandibular sulci, soft palate, buccal mucosa, and oropharynx. Additionally, the ventral surface of the tongue and the floor of the mouth are often affected. Aphthae appear as ulcer-like lesions, never as vesicles, and are isolated to single lesions without clusters.
2. *Coxsackie virus* (herpangina, hand-foot-and-mouth disease) might be considered in early differentiation.
3. Recurrent *herpes zoster* could be a consideration, but the lesions are unilateral and usually seen in older adults.

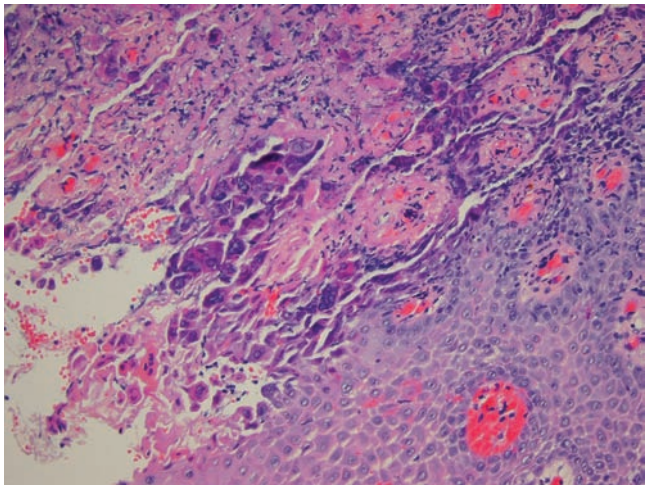

FIGURE 11.4. Histology of a herpetic lesion. (Courtesy of Dr. Yi-Shing Lisa Cheng.)

A careful health history will assist in differentiating the most likely possibilities.

Treatment and Prognosis: Palliative treatment with a soft diet, liquids that are nonacidic, and noncarbonated beverages are optimal. Cold foods help, such as ice cream or sherbet. Antipyretics and topical application of Benadryl elixir and Kaopectate 50–50% help to relieve pain to enable eating. Oral antivirals are not helpful once the lesions are present, although their use may prevent viral shedding and make the patient less infectious to others. The lesions usually resolve completely within 10 to 14 days. However, herpesviruses may follow a recurring pattern. (See Clinical Protocol #8 on treating intraoral herpes.)

NAME: Secondary or recurrent herpes simplex infections

Etiology: Recurrent infections are caused by reactivation of the latent virus. The event that causes the reactivation, or triggering event, is usually one that causes an altered or a compromised immune system such as a cold, fever, sunburn, emotional stress, trauma, pregnancy, infection, debilitation, menstruation, systemic disease, and possible allergies. In the oral cavity, activation may be precipitated by manipulation of tissues as in scaling and root planning or periodontal surgery.

Method of Transmission: The virus becomes reactivated and produces a recurrent infection. The virus cannot be considered transmitted in the strict sense of the term; however, the virus particles found in the recurrent lesions are active and can be transmitted to other individuals and to other areas of the affected individual's body (self-inoculation). Using cotton swabs and gloves when applying ointments is important in keeping the vesicles from spreading.

Epidemiology: Recurrent infections affect 20 to 40% of individuals after the primary infection.

Pathogenesis: This is a latent infection following the primary infection. When the dormant virus in the nerve ganglion is activated, it moves along the trigeminal nerve usually to the place of initial inoculation and infects the epithelial cells of the mucosa, creating vesicular lesions. As a result, the whole cycle begins again.

Extraoral Characteristics: Extraoral characteristics could be evident at the time of an outbreak, and clusters of vesicles would be seen only at this time, unless there is some scar formation due to extensive outbreaks.

Perioral and Intraoral Characteristics: These lesions initially appear as clusters of vesicles on the vermilion border, perioral skin, or less commonly on keratinized intraoral surfaces. When occurring on the lip and perioral areas, they are termed **herpes labialis.** Figure 11.5A depicts early herpetic lesions on the lip. Intraoral lesions appear unilaterally as very small vesicles on the palatal or attached gingiva. When the lesions occur on the lip, they are often referred to as cold sores or fever blisters, but the correct term is herpes labialis. The vesicles quickly rupture and leave ulcers that crust and usually heal without scarring in 7 to 14 days. Figure 11.5B shows vesicles on the lip in a later stage, beginning to heal and crust.

Distinguishing Characteristics: There are often localized, **prodromal symptoms** prior to a vesicle appearance such as burning, tingling, or pain before any eruption. Patients become very aware of these symptoms and can usually predict an outbreak of lesions. This is helpful in using ointments before the actual lesions appear.

Significant Microscopic Features: Histology of a herpes simplex infection reveals ulceration with fibrin exudates and acantholytic epithelial cells (**Tzanck cells**).

Dental Implications: When lesions are present, routine dental care should be postponed to prevent patient discomfort and spread of the virus. The lesions should be completely healed with no exudate apparent.

Differential Diagnosis: Herpes labialis is usually very distinct in appearance; however, early lesions may not appear as vesicles, but rather as skin irritations or raised areas on the lip. Careful questioning of the patient will usually provide the information needed to make a clinical decision.

1. *Impetigo*—a history of lesions should aid in differentiating the occurrence (see Chapter 23).
2. Intraorally, *recurrent aphthous stomatitis*—ulcerations tend to be less numerous, single rather than coalescing, and larger. Ulcerations usually occur on nonkeratinized tissues (see Chapter 12) and are ulcer-like with cratering.

Treatment and Prognosis: Herpes labialis antiviral topical, over-the-counter ointments or creams may reduce the duration and may stop some lesions from developing, if applied early, before replication of the virus occurs. Patients are often aware of the initial sensations associated with outbreaks and can intervene at an early stage before the replication is in full force. Always instruct patients to use a cotton applicator, rubber glove, or finger cot to reduce the potential for transmitting the virus to other parts of the body or to other individuals. Instruct the patient to avoid sunlight exposure when possible and to use a lip balm of SPF 15 or higher to protect the tissue. Unless the topical agent is applied during the prodromal phase before replication is well under way, it is of little benefit. Systemic antivirals may intercept the replication of the virus before the lesions develop.

Intraoral lesions—dental treatment may alter the patient's system so that the virus is reactivated. This is

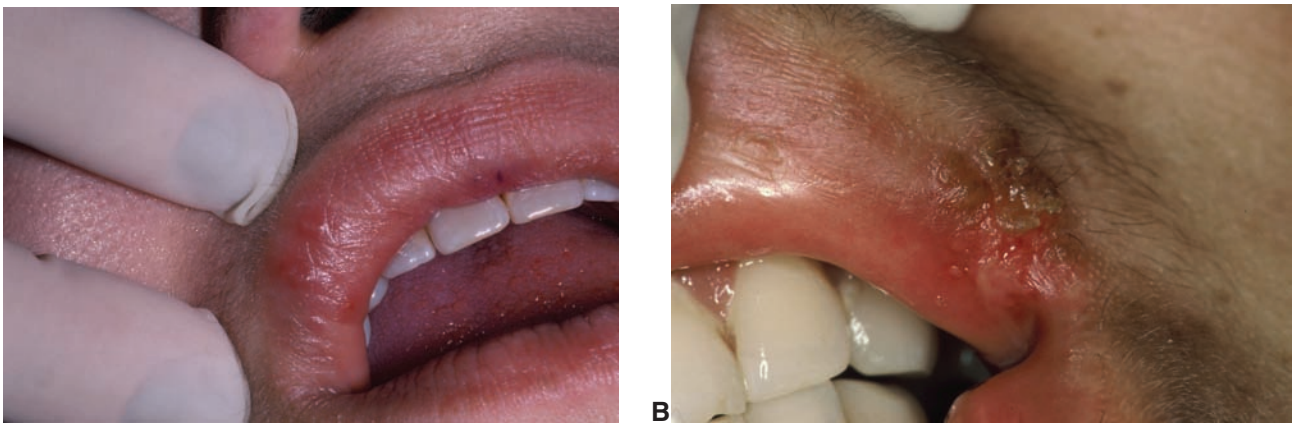

FIGURE 11.5. A. Early herpes lesions, a beginning herpetic lesion of the lip. **B.** Herpes labialis lesions at the commissure and upper lip area. (Courtesy of Dr. Michael Brennan.)

especially true if the patient has a history of developing ulcers after scaling and root planning or anesthetic injection. The use of systemic antivirals starting just before the dental treatment may intercept the lesions. Intraoral vesicles are usually very delicate and the clinician usually does not see the patient until ulceration has occurred. Therapy may shorten the duration of lesions, but success is more predictable if treatment is provided in the prodromal stage. The lesions are self-limiting and will resolve within 7 to 14 days. Using the antiviral medications when prodromal signs first occur is the most effective way to reduce or eliminate the outbreaks. Counseling the patient to use a lip balm with sunscreen and to avoid trigger mechanisms may help to limit the frequency of outbreaks.

Other Forms of Herpes Simplex Infection

Herpes infection can occur in other areas of the body such as on the fingers, eyes, nose, and skin areas when there is a break in the mucosa or mucosal lining. Safety glasses are mandatory for working in any area where there may be exposure to splash, aerosols, and debris from scrubbing any type of instrument or conducting any laboratory work. Safety goggles with side shields are a standard in the infection protocol and certainly crucial to avoid any potential contamination of the clinician's eye area. Many clinicians use a full, clear face shield to combat any debris from contaminating the face and neck area. Be sure to hold the face shield up to a light after the treatment of a patient and observe the amount of spatter on the shield. After doing so, a clinician will usually be sold on the benefit of using these devices. Of course, cleaning of the shield in between patients is crucial in maintaining infection control.

Herpetic Whitlow. The same HSV as those discussed in the previous sections causes **herpetic whitlow**. However, the infection occurs on the terminal segment of a finger (Fig. 11.6). The virus can leave the infected individual debilitated for weeks at a time. Herpetic whitlow usually occurs as a primary infection, but cyclic recurrence has been described. Health care workers are susceptible, especially when working in the mouth. In previous years, before the infection control standards of gloves were mandated, dental personnel were especially vulnerable. The HSV causing herpetic whitlow can be transferred and cause infection to other areas of the body such as the mouth, nose, and eyes or any other mucosal lining.

Ocular Herpes. Ocular herpes is an HSV infection, usually caused by autoinoculation. Although relatively rare, it may result from touching a herpetic lesion elsewhere and then touching the eye. There is, of course, a real danger of ocular herpes from any splash that may enter the eye from aerosols or debris during dental procedures. This is very serious and can result in blindness. The child seen in Figure 11.7 has exposed his eye to herpes and exhibits obvious lesions in the mouth and perioral tissues. Lesions are seen on the mouth and periorally with bleeding.

Herpes Simplex Virus and Genital Herpes. This form of herpes is transmitted in genital secretions, producing genital ulcerations. The practice of oral sex in the patient population has increased the likelihood of transmission of HSV to both the oral and genital tissue areas. For the purpose of this book, we mention this fact, although there is no way to differentiate the types without very sophisticated laboratory and histologic tests. Research supports the transmission of herpetic viruses through oral sex. Oral sex is also implicated in certain head and neck cancers caused by the human papilloma viruses (HPV), which is discussed in Chapter 16.

FIGURE 11.6. Herpetic whitlow. (Courtesy of Dr. Peter Jacobsen.)

FIGURE 11.7. Ocular herpes. (Courtesy of Dr. Peter Lockhart.)

APPLICATION **11.1**

Are You Providing Herpes Instructions?

All individuals who experience herpetic lesions should be warned of the possibility of transferring the virus to the eyes and to any mucosal lining or to other individuals. They should use caution not to touch the lesions with unprotected fingers, and they should wash their hands thoroughly after each application of topical medication. The herpes simplex virus (HSV) is delicate, but it can live on surfaces and in droplets for up to 2 to 3 hours, and standard infection control procedures must be followed to protect the clinician, patient, and subsequent patients in the dental office. The patient should be warned to keep household items, counters, faucets, and surface areas clean so that other family members are not infected.

NAME: Primary varicella–zoster (chickenpox)

Varicella is the original infection (chickenpox); herpes zoster (shingles) occurs when the virus is subsequently reactivated. We have discussed the HHV types 1 and 2, caused by the HSV. As discussed earlier in the chapter, there are eight known HHV type categories. The HHV-3 is known as the VZV. As with types 1 and 2, HHV-3 has some oral manifestations and is covered in this section as well.

Etiology: The HHV-3, or VZV, is the causative agent of primary varicella infection, better known as chickenpox.

Method of Transmission: Transmission occurs through air droplets or direct contact with lesions. This is a highly contagious disease when lesions are present.

Epidemiology: Young children are most often affected, but the disease can occur in adults who have never been exposed to the virus. Males and females are affected equally. Figure 11.8A shows a female with a primary varicella infection.

Pathogenesis: The virus normally infects the respiratory tract, and it is carried through the body via the bloodstream into the epidermis. At this point, viral replication begins to destroy the epithelial basal cells. After a 2-week incubation period, symptoms begin to appear. The virus can be transmitted approximately 2 days before the appearance of the rash and until all lesions are crusted, with no detectable drainage. The disease resolves in 2 to 3 weeks. The virus may migrate over sensory nerves to lie dormant in ganglia until triggered later, much like the HSVs. If this occurs, the virus remains in a latent stage in ganglia along the sensory nerves and may be reactivated years later to emerge as herpes zoster, or shingles, discussed in the next section.

Extraoral Characteristics: The symptoms usually begin with malaise, sore throat, and upper respiratory congestion. Fever and slight lymphadenopathy usually precede or occur concurrently with a vesicular rash that appears on the trunk, head, and neck. The vesicles form pustules and then ulcers with an erythematous border. Figure 11.8B shows the skin lesions of primary varicella chickenpox. During the peak of the infection, new lesions continue to develop while older lesions are beginning to heal, so that one can observe lesions in all stages of development. The lesions are extremely pruritic, and it is difficult to keep the patient, usually a child, from scratching them. Often, scratching will introduce bacteria into the lesions, causing a secondary bacterial infection that usually results in scarring.

APPLICATION **11.2**

Are You Dressing the Part? Proper Attire

Excellent office protocol is crucial in adhering to good infection control practices for your work environment. Keeping abreast of current standards with methods of safety for both you and the patient is part of good work ethics and practice. As discussed, the HSV virus is easily spread, and any dental procedures must be postponed when infection is active. Infection control issues need to be maintained to protect the health of both the practitioner and patient. The following are required for adequate safety protection:

- Goggles with shields
- Full-face shields
- Clinic wear consisting of long sleeves that are bound at the wrists
- Totally washable garments
- Overgarments that are changed between patients
- Mask and gloves

Most of these are always mandatory. In some practices, street clothing with open jackets are worn, and this type of office wear does not adequately protect either the patient or the practitioner. The realization that anything worn around a patient or spattered-on clothing worn away from the office will endanger others is key to confining any viral or infectious agents. Contracting ocular herpes or any other form of herpes can be life changing for you, your family, and the patient.

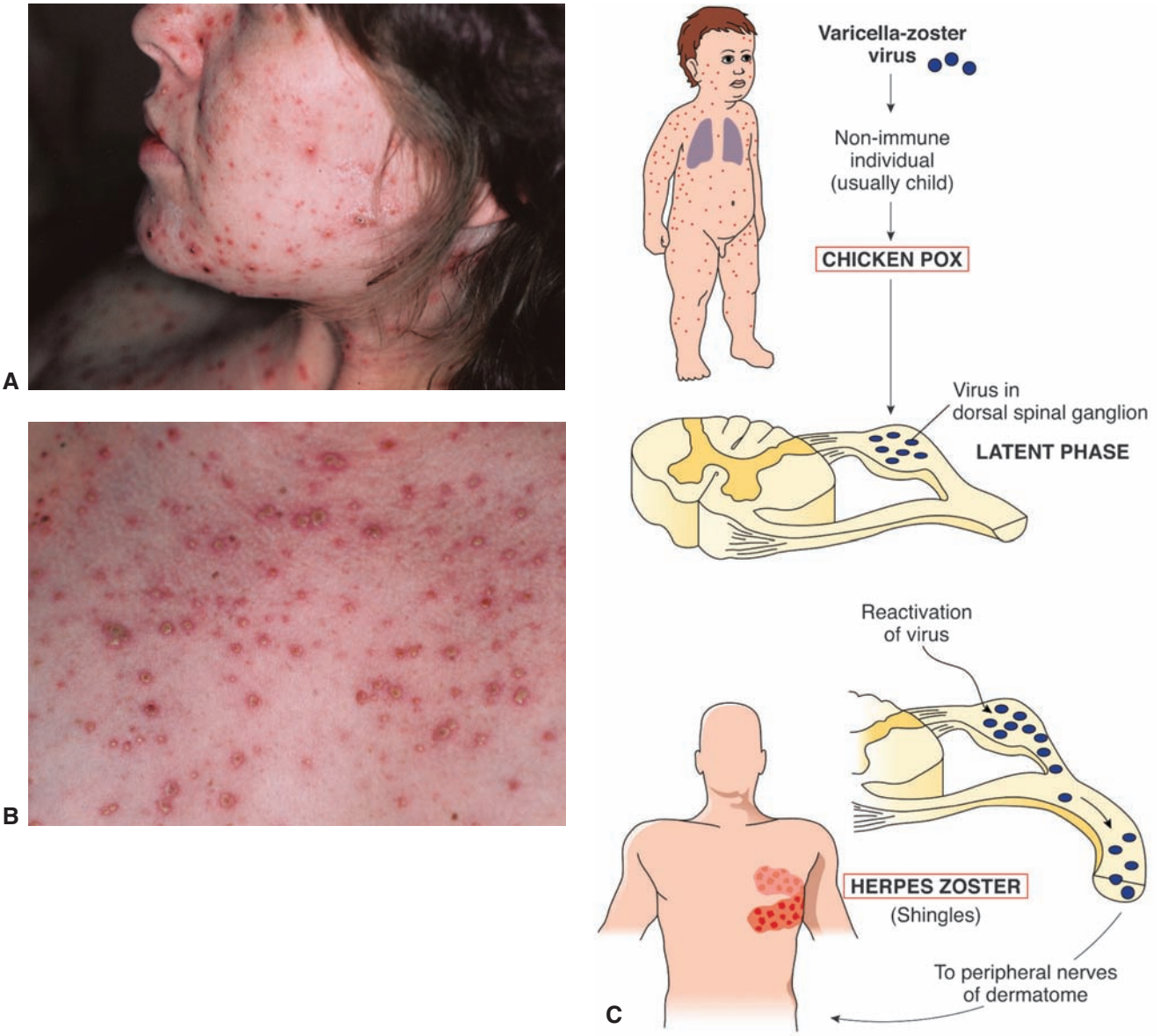

FIGURE 11.8. Chickenpox. **A.** Skin lesion of varicella (chickenpox). (From Sweet RL, Gibbs RS. Atlas of infectious diseases of the female genital tract. Philadelphia: Lippincott Williams & Wilkins, 2005.) **B.** Skin lesion of chickenpox. (From Sweet RL, Gibbs RS. Atlas of infectious diseases of the female genital tract. Philadelphia: Lippincott Williams & Wilkins, 2005.) **C.** Progression of varicella and herpes zoster virus—the progression of varicella to shingles. (From Rubin E, Farber JL. Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 1999.)

Perioral and Intraoral Characteristics: Cutaneous lesions may form anywhere in the head and neck region and appear identical to the lesions found on the trunk and the extremities. Vesicular intraoral lesions are usually found on the lips, hard palate, and the buccal mucosa. The lesions will heal without scarring in most cases. Figure 11.8C depicts the progression of VZV and, subsequently, shingles or herpes zoster.

Distinguishing Characteristics: This disease presents with a wide range of symptoms, and, often, the infection is subclinical or may be a minor rash of only a few lesions and some upper respiratory symptoms. Occasionally, the disease is so severe that the patient has to be hospitalized to maintain hydration and body temperature. Usually, the disease manifests somewhere between these extremes. The intense pruritus, clinical presentation, and self-limiting course of the disease usually distinguish it from other conditions.

Significant Microscopic Features: Superficial intraepithelial vesicles

Dental Implications: Treatment should not proceed until the person is completely healed without any visible exudates in any of the lesions, both orally and extraorally.

Differential Diagnosis:

1. HSV type 1—Painful lesions are not present in chickenpox.
2. Pruritus may be present with chickenpox and hand-foot-and-mouth disease.

3. There are vesicles on the trunk with chickenpox.
4. Aphthae would not be a good differential since the oral lesions are not usually painful in chickenpox. Aphthae occur on nonkeratinized epithelium as single, large ulcerations.

Treatment and Prognosis: Palliative care is suggested, with topical preparations to relieve pruritus. Nonaspirin antipyretics are recommended for any discomfort. This infection is self-limiting, with complete resolution of the lesions in 2 to 3 weeks. However, complications are occasionally associated with this disease including the following:

- Encephalitis, Reye syndrome, and pneumonia can occur.
- Infection during pregnancy may cause spontaneous abortion or congenital birth defects.

Vaccines are provided for children and are usually given in the combination MMR, commonly provided as childhood immunizations. Adults may reactivate the virus that leads to herpes zoster (shingles), discussed below. A vaccine recently developed for the prevention of shingles may be used for older adults (over 60 years of age). This new prophylactic procedure has been shown to be cost-effective in this age group. However, patients are usually checked to be sure that they have had chickenpox previously.

NAME: Secondary varicella–zoster (shingles or herpes zoster)

Etiology: Shingles is caused by reactivation of the latent VZV.

Method of Transmission: Shingles is caused by a latent viral infection, and there is no method of transmission other than that which caused the primary infection. However, the lesions in shingles contain active viral particles, and contact with them by a susceptible person can cause the primary disease, which is chickenpox. The patient should be cautioned to avoid contact with persons at high risk such as immunocompromised persons and pregnant women, since the patient is contagious and may infect other individuals. Anyone in an altered immune state and anyone who has not been exposed to varicella could be at risk.

Epidemiology: Herpes zoster is seen most often in adults, especially the elderly, and slightly more often in males than females.

Pathogenesis: The virus may migrate over sensory nerves to lie dormant in ganglia until triggered later, much like the HSVs. Reactivation of latent VZV stems from the dorsal ganglion or the trigeminal ganglion. One of the three branches of the trigeminal nerve may be affected: the ophthalmic branch, the maxillary branch, or the mandibular branch. Figure 11.9A illustrates the nerve areas affected by secondary VZV. The triggering factors may include stress, compromised immune system, debilitating disease states, etc. Prodromal symptoms of pain or paresthesia are common. The unilateral vesicular lesions develop 2 to 4 days later and may last for 2 to 3 weeks.

Extraoral Characteristics: The disease usually presents unilaterally over the sensory nerves of the head, neck, and trunk as a vesicular rash that is extremely painful. The vesicles rupture and crust in a manner similar to that of chickenpox. Along with the rash, there may be fever, pain, malaise, and lymphadenopathy.

Perioral and Intraoral Characteristics: Intraoral presentation is unilateral and consists of small vesicular eruptions on any mucosal surface or on the palate (Fig. 11.9B).

Distinguishing Characteristics: Shingles may be diagnosed clinically when the unilateral distribution of skin lesions is evident. Additionally, the oral lesions and the distinct halt of the lesions at the midline are very characteristic of the disease.

The virus does not migrate far beyond the area of skin or mucous membrane supplied by the infected nerve. Figure 11.9C demonstrates the demarcation of the lesions, which subside at the midline of the face.

Significant Microscopic Features: These are the same as those of a primary infection.

Dental Implications: Shingles is a self-limiting condition and should resolve in 2 to 3 weeks. However, 14% of affected individuals may experience **postherpetic neuralgia (PHN)** causing persistent and often severe pain (Boivin et al., 2010) lasting 90 days after rash onset. PHN usually resolves within 2 months but may follow a prolonged course and last for years. Other infrequent complications include **Ramsay Hunt syndrome**, which affects the facial nerve (facial paralysis, diminished hearing, and vertigo) with vesicles on the tongue, palate, or ear. Blindness may occur, which is due to involvement of the ophthalmic division of the trigeminal nerve. One rare and serious complication of herpes zoster is spontaneous tooth exfoliation and necrosis of the mandible. PHN is a concern with the development of shingles. Antiviral therapy initiated within 72 hours of rash onset has been shown to accelerate rash healing, reduce duration of acute pain, and affect PHN. Additionally, analgesics, antidepressants, and anticonvulsants are often required in the management of severe cases of PHN. Common antiviral medications that may be used are acyclovir (Zovirax), valacyclovir (Valtrex), and famciclovir (Famvir).

Differential Diagnosis: The pruritic rash is characteristic of other skin disorders in the early stages, such as:

1. Herpes simplex
2. Impetigo
3. Rubella
4. Rubeola

Additionally, a laboratory diagnostic test may be needed when atypical lesions are present or when the clinician is

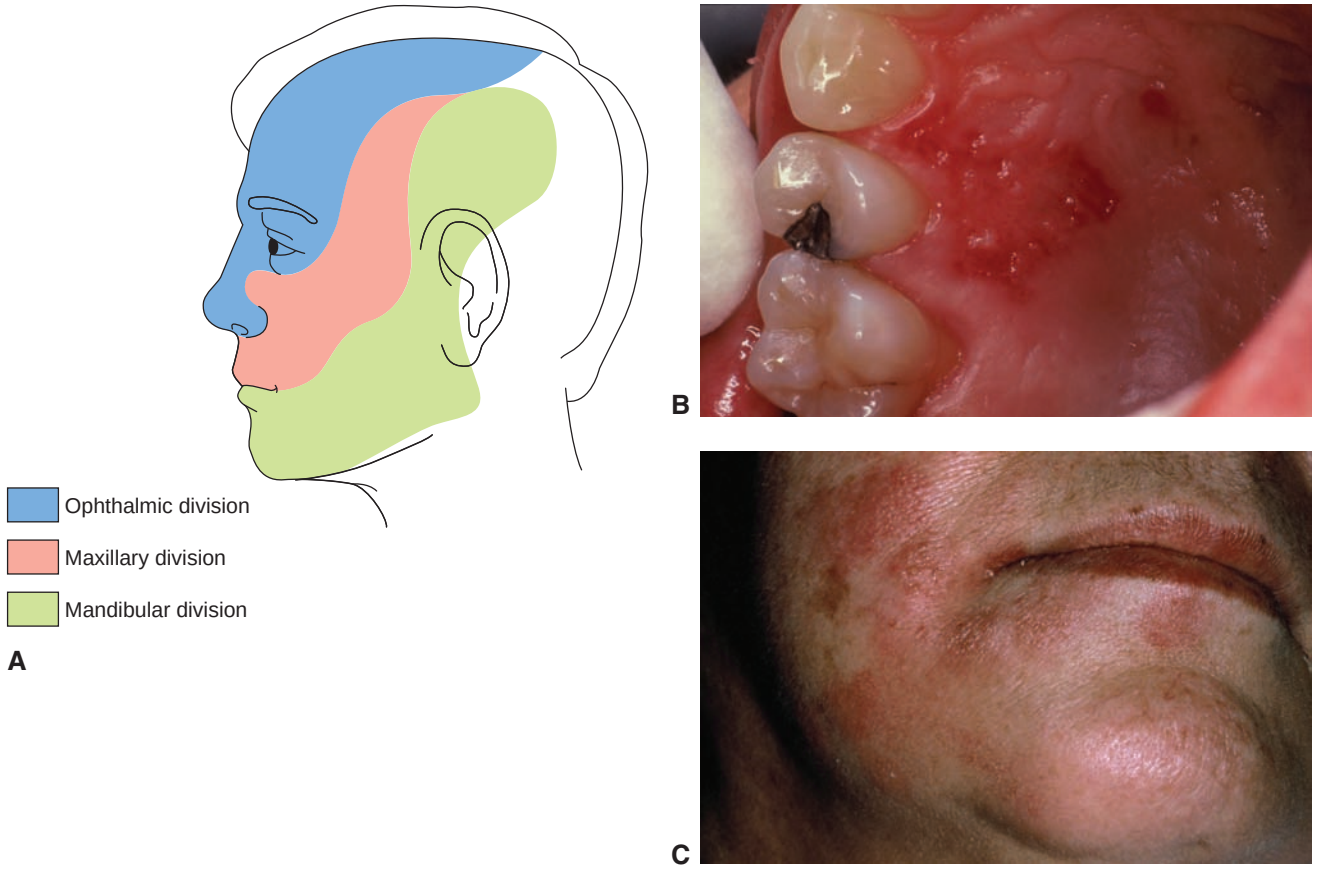

FIGURE 11.9. Varicella–zoster. **A.** Trigeminal nerve branches. **B.** Herpes zoster shingles in the lingual palatal region. (Courtesy of Dr. Michael Brennan.) **C.** Facial shingles from the ramus to the midline.

unclear whether another entity may be involved. Direct fluorescent staining is diagnostic in most cases.

Treatment and Prognosis: Routinely, patients are seen by their physicians for treatment; however, dental personnel are often involved initially when oral pain is reported.

The recommended therapy includes isolation, local management of the skin lesions, controlling pain, antiviral medications, and treatment of herpetic neuralgia. Palliative procedures are recommended with antiviral agents to reduce viral shedding. Topical agents such as patches are sometimes recommended for skin lesions depending upon the severity of pain. This may shorten the duration and decrease the probability of PHN (see below). Oral lesions should be treated in a palliative way with soothing mouth rinses and/or topical anesthetics. The vaccine for varicella is the prime way of avoiding chickenpox and also shingles later in life. The shingles vaccine has been available since 2006 in the United States (Zostavax, Merck & Co., USA). Individuals over 60 years of age should talk to their physician about the vaccine. In some cases, the vaccine may not be appropriate, such as in those who are pregnant or have immune system problems, allergy concerns, cancer, or those receiving treatment for cancer.

Coxsackievirus Infections

Numerous viruses exist in the environment that can produce rashes and vesicles. The following section discusses some of the most common that the clinician may see in a dental practice. Picornaviruses are part of the genus Enterovirus. These viruses cause disorders with a wide range of clinical manifestations including cutaneous and neurological disease. Coxsackie is an enterovirus (EV71) that causes human herpangina and hand-foot-and-mouth disease.

NAME: Hand-foot-and-mouth disease

Etiology: The coxsackie A-16 virus and other coxsackievirus A and B strains cause **hand-foot-and-mouth disease.** Figure 11.10A–C depicts the lesions associated with hand-foot-and-mouth disease.

Method of Transmission: The virus is transmitted through airborne and oral/fecal routes, fomites, and respiratory droplets. Replication of the virus occurs in the lymphoid tissue of the oropharyngeal cavity, the small bowel, and regional lymph nodes. Infection confers immunity against reinfection by that particular strain; however, the person may be infected with other strains later. Hand-foot-and-mouth disease is highly contagious. Viral shedding can continue for up to 2 weeks

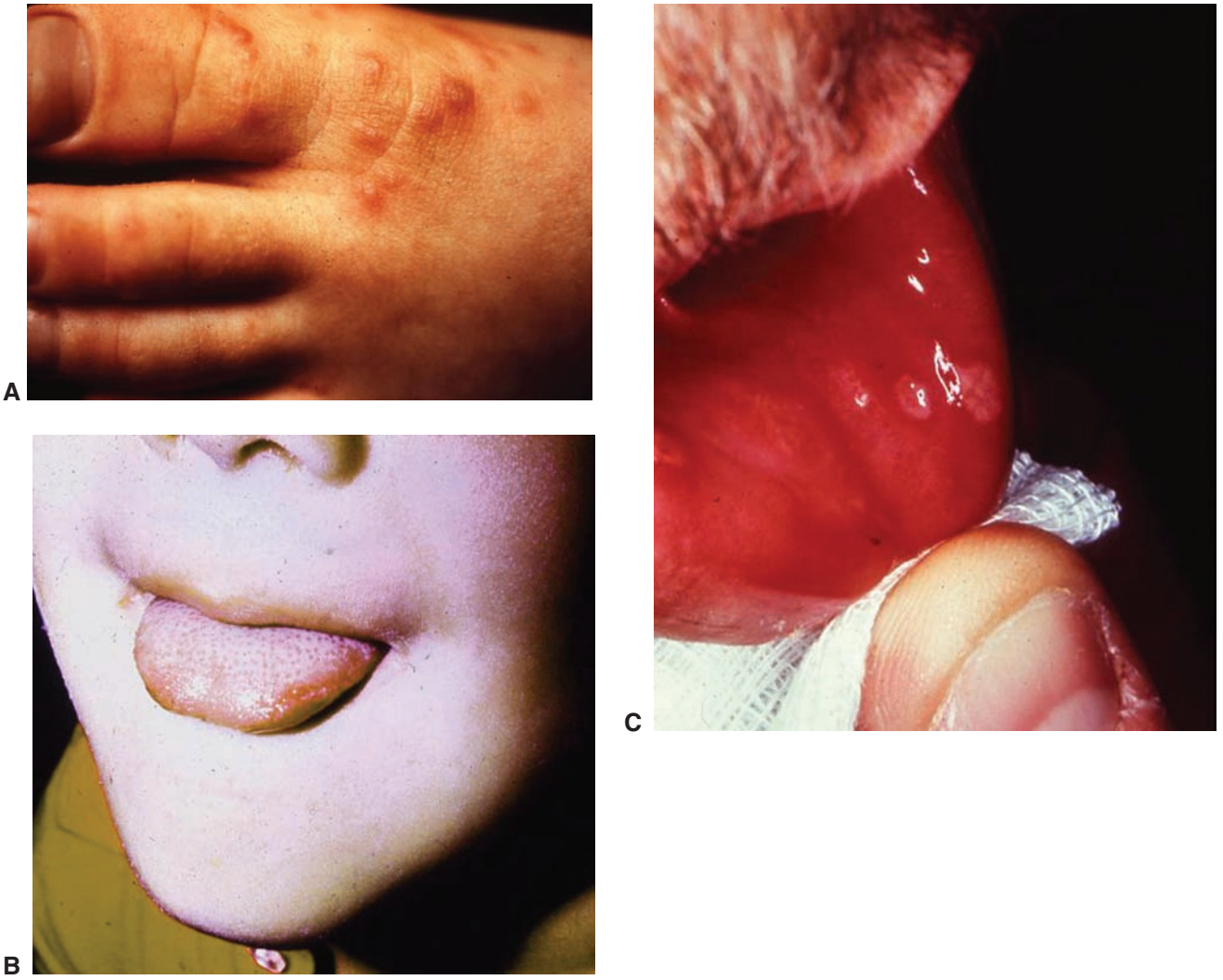

FIGURE 11.10. Hand-foot-and-mouth disease. **A.** Vesicles on the foot of a young adult. **B.** Vesicles on the tongue of a child. **C.** Vesicles with severe ulceration of the mucosa in an adult. (Courtesy of Dr. T.D. Rees.)

after the acute infection and the virus can be isolated from stool samples for up to 11 weeks (Solomon et al., 2010).

Epidemiology: This disease especially affects children under 5, who are vulnerable because of the contact with other children and the numbers who are in schools and daycare centers. Males and females are affected equally.

Pathogenesis: Incubation is 4 to 7 days, and the disease tends to occur in the summer or early fall. Resolution of the clinical symptoms occurs in 1 to 2 weeks.

Extraoral Characteristics: A maculopapular rash occurs on the soles of the feet and the palms of the hands. These lesions develop central vesicles that may or may not rupture and become crusted before healing. Systemic involvement includes fever, sore throat, malaise, and lymphadenopathy.

Perioral and Intraoral Characteristics: Intraoral lesions usually precede the cutaneous rash and may appear on any mucosal surface. The lesions form vesicles that rupture, ulcerate, and become very painful.

Distinguishing Characteristics: Vesicles and ulcers occur on the buccal mucosa, tongue, and palate orally, with external lesions on the soles of the feet, palms of the hands, and fingers and toes. The location of the lesions usually provides a good indication of the disease.

Significant Microscopic Features: Intraepithelial vesicles precede shallow ulcerations.

Dental Implications: The oral lesions cause pain and difficulty with eating and swallowing.

Differential Diagnosis: The lesion distribution is usually diagnostic, with the prevalence to the palms of the hands and soles of the feet.

1. Varicella may initially be a consideration.
2. Primary herpetic gingivostomatitis may be considered as well.

Treatment and Prognosis: Treatment is directed toward symptomatic relief. Antipyretic agents and topical medications

for sore mouth are the treatments of choice. The prognosis is excellent, and no complications would be expected.

NAME: Herpangina

Herpangina may arise from a number of other types of coxsackievirus A strains. The patient will still be susceptible to other strains of the virus and may contract the disease again. Patients usually complain of a sore throat with fever, loss of appetite, abdominal pain, and vomiting. Depending upon the length of time and severity of the symptoms, the patient may complain of varying degrees of discomfort.

Etiology: Herpangina is a disease also caused by the coxsackievirus and specifically, the A-16 coxsackievirus. Because of the prevalence of a younger age group, it is often found in schools and daycare centers, and it is easily transmitted. Figure 11.11 depicts lesions in the posterior oropharynx region.

Method of Transmission: Herpangina is easily transmitted via an oral/fecal route.

Epidemiology: Children are most susceptible, with an equal ratio of males and females.

Pathogenesis: Incubation is 4 to 7 days, and the disease tends to occur in the summer or early fall. The onset of symptoms is sudden, with sore throat, dysphagia, fever, headache, and sometimes vomiting. Resolution of the lesions occurs in 1 to 2 weeks; systemic symptoms usually dissipate in 2 to 3 days.

Extraoral Characteristics: Oral lesions are found in the posterior regions of the mouth, soft palate, anterior and posterior pharyngeal pillars, and tonsils. Herpangina presents with a diffuse reddening of the tissues and the appearance of vesicles that rupture and ulcerate.

Perioral and Intraoral Characteristics: Herpangina is characterized by vesicular lesions ranging in size from 1 to 2 mm.

Distinguishing Characteristics: The vesicles of herpangina are small vesicles and ulcerations in the pharyngeal area.

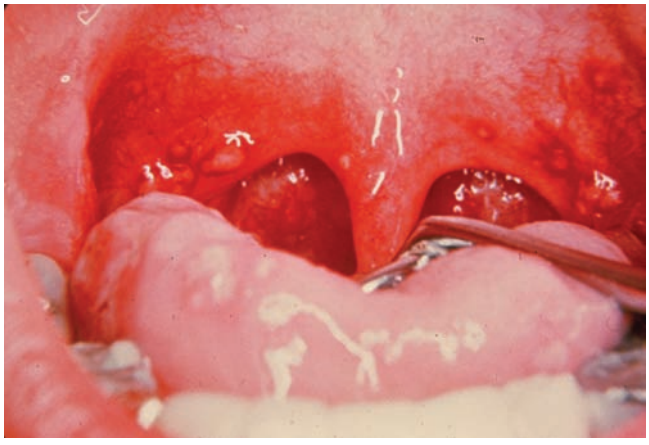

FIGURE 11.11. Herpangina. (Courtesy of Dr. John Jacoway.)

Significant Microscopic Features: Not applicable

Dental Implications: Dental treatment needs to be postponed until all vesicles and ulcerations are healed.

Differential Diagnosis: Diagnosis usually is made from historical and clinical information with little difficulty. Some physicians state that herpangina may appear as strep throat in some cases because of the intense red color.

Treatment and Prognosis: Palliative treatment is recommended and may or may not be required. Excellent prognosis; complications are rare.

Acute Lymphonodular Pharyngitis

Also caused by the coxsackievirus, acute lymphonodular pharyngitis (ALP) is a very rare condition that is also characterized by a sore throat, just as herpangina. Small nodules in the pharyngeal area and the tonsillar pillars characterize the disease. ALP is caused by a different strain of the coxsackievirus and may vary in appearance from vesicle-like to nodular.

Paramyxoviridae virus infections

NAME: Rubeola (measles)

Etiology: The virus originates from the Paramyxoviridae family. Measles **(rubeola)** has seen a sharp decline, since most children receive the MMR vaccine in early childhood.

Method of Transmission: Measles is airborne and spread through respiratory droplets.

Epidemiology: Children and young adults. There is an equal male-to-female ratio.

Pathogenesis: Most cases arise in the winter and spring. The incubation period is 10 to 12 days, after which prodromal symptoms occur consisting of fever, malaise, upper respiratory congestion, cough, and conjunctivitis. An erythematous maculopapular rash appears after several days and lasts for 4 to 7 days.

Extraoral Characteristics: The dermal erythematous rash begins on the face and moves downward to cover the trunk and extremities.

Perioral and Intraoral Characteristics: Characteristic lesions called **Koplik spots** are found intraorally on the buccal and labial mucosa. These precede the extraoral rash and are considered pathognomonic. They appear as small, bluish white spots on an erythematous background. In severe cases, pitting of the enamel (enamel hypoplasia) in developing teeth may occur.

Distinguishing Characteristics: The intraoral Koplik spots along with the cutaneous rash are usually diagnostic. Figure 11.12 depicts Koplik spots.

Significant Microscopic Features: Epithelial cells become necrotic. Additional tissue tests may be used to determine the presence of viral antigens.

FIGURE 11.12. Measles (rubeola). Koplik spots of rubeola. (Courtesy of Dr. James Sciubba.)

Dental Implications: All dental work should be postponed until the virus has been eliminated.

Differential Diagnosis: The diagnosis is based on clinical findings both externally and orally.

Treatment and Prognosis: The treatment is palliative with nonaspirin antipyretics. Complications may include pneumonia and encephalitis. Death may occur in severely immunocompromised individuals.

Togavirus Infections

NAME: Rubella (German measles)

Etiology: The togavirus and not the Paramyxovirus (as discussed in rubeola forms of measles) causes the German measles, or rubella. The togavirus replicates in the oropharynx and regional lymph nodes and spreads through the bloodstream to skin and distal organs. It can cross the placental barrier, so avoidance of exposure by pregnant women is crucial, since known birth defects have occurred. The birth defect rate is at the highest when the mother is exposed during the first trimester of pregnancy.

Method of Transmission: German measles are highly contagious and spread through respiratory droplets. A vaccine was developed in 1969, reducing the incidence of the virus.

Epidemiology: German measles are most commonly found in children or adults who have not been vaccinated or exposed to the virus. There is an equal predilection. The disease usually occurs in the spring, with a 2- to 3-week incubation period.

Pathogenesis: After an incubation period of 12 to 24 days, a mild erythematous rash occurs, accompanied by low-grade fever. The rash usually disappears within 3 to 5 days. Complications during pregnancy include spontaneous abortion or fetal injury causing one or more features of the congenital rubella syndrome (deafness, heart disease, cataracts, encephalopathy, mental retardation, and others). Severe complications are more likely if the mother is infected during the first trimester of pregnancy.

Extraoral Characteristics: Patients usually complain of malaise, fever, nausea, and poor appetite. Lymphadenopathy is evident, with red and pink papules on the body.

Perioral and Intraoral Characteristics: Small, discrete, dark-red papules on the soft and hard palate occur in some cases, and these lesions are known as **Forchheimer signs.**

Distinguishing Characteristics: Forchheimer signs may be visible in the soft palate region and are considered an early sign of the infection.

Significant Microscopic Features: Serologic analysis is required to confirm.

Dental Implications: Not applicable

Differential Diagnosis:

1. With rubeola, the signs and symptoms are more severe and much more prolonged.
2. Hand-foot-and-mouth disease may appear more vesicle-like than rubella.
3. Herpangina may appear more vesicle-like than rubella.

Treatment and Prognosis: Nonaspirin antipyretic medications may be helpful in soothing the discomfort. With any signs of vesicles present either intraorally or extraorally, the patient should be sent to his or her physician. Airborne particles place staff members and subsequent patients at risk for coming in contact with an infectious disease. Pregnant women are highly susceptible.

Noninfectious Vesiculobullous Diseases: Autoimmune Diseases

This section discusses diseases of an autoimmune nature that have a vesiculobullous intraoral presentation. These diseases are difficult to distinguish on a clinical basis, and microscopic and immunofluorescence features must be determined to obtain a positive diagnosis. However, there are subtle clinical and historical differences that may lead the clinician to suspect one disease over the other possibilities. Multiple lesions that have a gradual onset and a chronic nonhealing course characterize them all. Cutaneous lesions may or may not be present.

NAME: Pemphigus vulgaris

Etiology: **Pemphigus vulgaris** is an autoimmune disease.

Method of Transmission: Since the disease is an autoimmune disease, there is no mode of transmission.

Epidemiology: There is no sex predilection. Pemphigus vulgaris generally affects patients in the fourth to sixth decades of life; however, the disease may occur in all age groups.

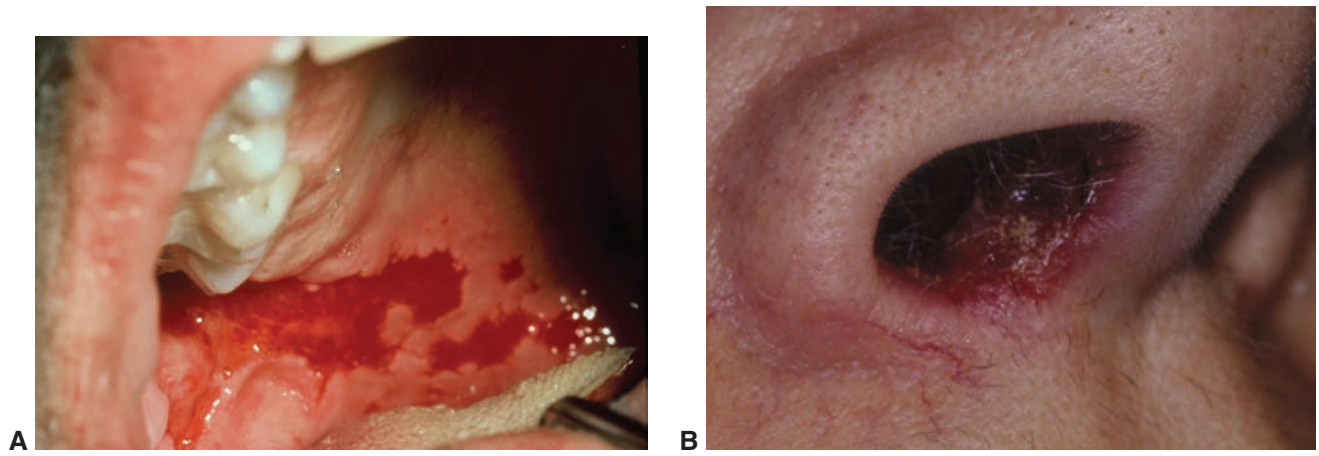

FIGURE 11.13. Pemphigus vulgaris. **A.** Stripping of the epithelial tissue in the posterior oral region. **B.** Pemphigus of the nose with ulceration and crusting. (Both slides courtesy of Dr. Terry Rees.)

Pemphigus is a term used to describe a group of chronic diseases with potential intraoral involvement, including pemphigus vulgaris, pemphigus vegetans, pemphigus foliaceus, pemphigus erythematosus, paraneoplastic pemphigus, and others.

Pemphigus vulgaris is by far the most common form of the disease. Individuals of Jewish or Mediterranean descent may be affected more frequently, and there may be a familial tendency for the disease.

Pathogenesis: Pemphigus vulgaris is associated with human leukocyte antigens A10, A26, Bw28, and DR4.

Extraoral Characteristics: Oral lesions may be the initial sign of pemphigus in over 50% of affected individuals, and virtually 100% of untreated individuals will develop oral lesions. These lesions begin as bullae, usually greater than 1 cm in size, that rupture quickly to form shallow ulcers covered by a gray pseudomembrane. The membrane can be removed to reveal an erythematous surface, as seen in Figure 11.13. The ulcers are painful and can be found on any mucosal surface. If untreated, the lesions persist and enlarge.

Perioral and Intraoral Characteristics: Lesions may be found on any epithelial surface including the skin, oral cavity, esophagus, larynx, pharynx, vagina, anus, and eyes.

Distinguishing Characteristics: **Nikolsky sign** is usually positive in affected patients. This sign is considered positive when the clinician can initiate bulla formation by stretching or rubbing the mucosa in a clinically unaffected area.

Significant Microscopic Features: Microscopically, intraepithelial clefting or acantholysis (cell separation in the stratum spinosum) with freely floating, rounded epithelial cells called **Tzanck cells** are characteristic, as seen in Figure 11.14. Irregularly arranged basal cells may have a tombstone-like appearance. There is also a positive direct and indirect immunofluorescence test (Fig. 11.5) Pemphigus features a separation of epithelial cells (**acantholysis**) caused by autoantibodies that attack a protein component of the desmosomes, which is the adhesion site between two epithelial cells. This protein component binds epithelial cells together (the intercellular cement) in stratified squamous epithelium. This leads to blister formation (bulla) and ulceration of affected tissues.

Dental Implications: An extensive team approach is needed to treat pemphigus, which invariably includes high-dose systemic corticosteroids and immunosuppressive agents. Oral lesions respond to a combination of systemic therapy and high-potency topical steroids such as fluocinonide. Effective oral hygiene is crucial. Alcohol-containing products and abrasive dental products may be harmful; however, use of non–alcohol-containing mouth rinses such as chlorhexidine mixed in water may be beneficial. Although not commercially available, these products can be prepared by compounding pharmacists and tend to be highly effective in treatment. Tooth-whitening agents should not be used because of their abrasive properties and ability to irritate the tissues. Recall appointment guidelines may include gentle débridement with minimal tissue manipulation. This may include multiple appointments to meet the therapeutic goal. Other procedures include taking clinical photographs for optimal monitoring and discontinuing flavoring agents. (See Clinical Protocol #6 for sensitivity to flavoring

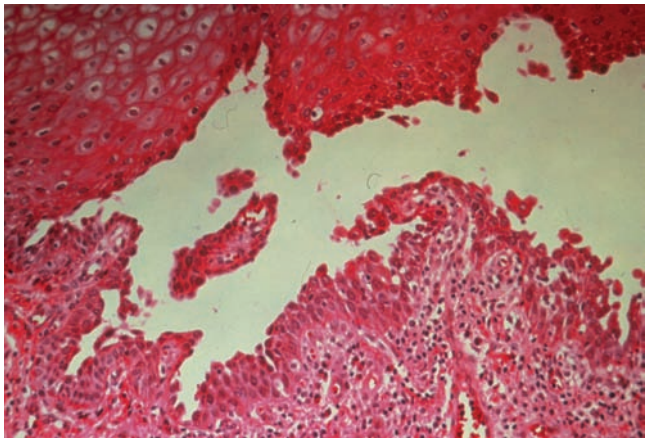

FIGURE 11.14. Pemphigus photomicrograph with Tzanck cells.

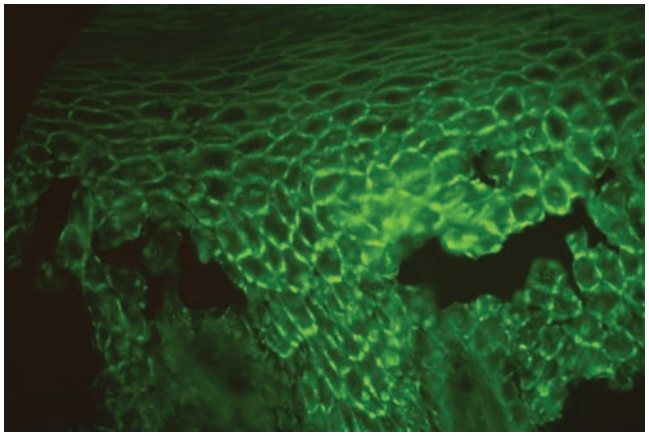

FIGURE 11.15. Immunofluorescence slide of pemphigus vulgaris. (Courtesy of Dr. Denis Lynch.)

agents.) Hydrogen peroxide and other ingredients found in dental hygiene products may be irritating to patients with mucosal disease, and spicy foods should be eliminated.

Differential Diagnosis: Any of the bullous conditions need to be considered:

1. Bullous pemphigoid
2. Pemphigus
3. Erosive lichen planus
4. Erythema multiforme
5. Discoid lupus erythematosus

Parker and MacKelfresh (2011) suggest some pertinent questions that should be considered by the clinician when attempting to differentiate an autoimmune blistering disease in the elderly patient.

- Are the blisters localized or widespread?
- Are the blisters cutaneous, mucosal, or mucocutaneous?
- Is a particular pattern (annular, linear, clustered, etc.) evident?
- Is the surrounding or underlying inflammation or edema present?
- Are the lesions pruritic or painful?

With any nonhealing chronic condition, there is always the possibility that changes have occurred since the last maintenance visit. The clinician should always entertain the possibility that, even though a diagnosis was made previously, a patient may have a new disease or the existing disease has taken a different course. This is especially true for any chronic mucosal disease. Chronic inflammation of the tissues may lead to a more serious state, such as carcinoma. Any changes need to be evaluated, and new testing may be warranted. Intraoral photographs that can be compared are crucial in evaluating all mucosal diseases and should be used.

The presence or absence of skin lesions should help with the differential diagnosis; however, definitive diagnosis must be based on microscopic features as well as immunofluorescence results. A biopsy is essential in determination with immunostaining.

Treatment and Prognosis: Pemphigus vulgaris is a potentially life-threatening condition, and it is imperative that the patient receives medical care. Unfortunately, the medications used to treat the condition may induce adverse side effects or systemic complications. For example, complications of chronic steroid therapy may include diabetes mellitus, hypertension, adrenal suppression, weight gain, osteoporosis, peptic ulcers, severe mood swings, and diminished resistance to infectious agents. If left untreated, there is a 60 to 80% mortality rate; if treated, the mortality rate is 5 to 10%.

Pemphigoid

Pemphigoid represents a group of chronic, vesiculobullous, pemphigus-like diseases that affect skin and mucous membranes. The oral cavity may be involved in all forms of pemphigoid, and in many instances, it may represent the only site of lesions. On some occasions, pemphigoid lesions may be drug induced by such medications as carbamazepine, clonidine, or penicillamine.

NAME: Mucous membrane pemphigoid (cicatricial pemphigoid, benign mucous membrane pemphigoid)

Etiology: When affecting the gingiva, the term **desquamative gingivitis** is sometimes used. Antibodies, usually IgG but sometimes IgA, target subepithelial components of the basement membrane zone. Scarring and fibrosis result from the basal destruction and separation.

Method of Transmission: Mucous membrane pemphigoid (MMP) is idiopathic and classified as an autoimmune disease.

Epidemiology: The disease affects older middle-aged (usually fifth decade) and elderly individuals. Pemphigoid is rare in children. Females are affected more than males in a ratio of 2:1. The elderly may be at special risk, affecting the 60- to 80-age range. No specific disease states predispose a person to pemphigoid.

Pathogenesis: MMP appears to be caused by antibodies that target the basement membrane and cause weakening of the attachment to the underlying connective tissues. In this disease, bulla formation occurs in the subepithelial area between the connective tissue and the basement membrane. Figure 11.16 shows the histology of this disorder, with separation of the basal cell layer from the underlying connective tissue. The most common sites of pemphigoid involvement are the oral mucosa followed by the conjunctival mucosa.

Extraoral Characteristics: Various other mucous membranes may be involved, including the genitalia, and eye and localized skin bulla occasionally occur. Lesions may also be found on the skin, nares, rectum, urethra, and esophagus. The bullae of MMP are short-lived; they break quickly and desquamate, leaving a raw erythematous or ulcerated surface. Scarring rarely occurs in the oral cavity, but on the skin and ocular mucosa, scarring is a major factor of the disease.

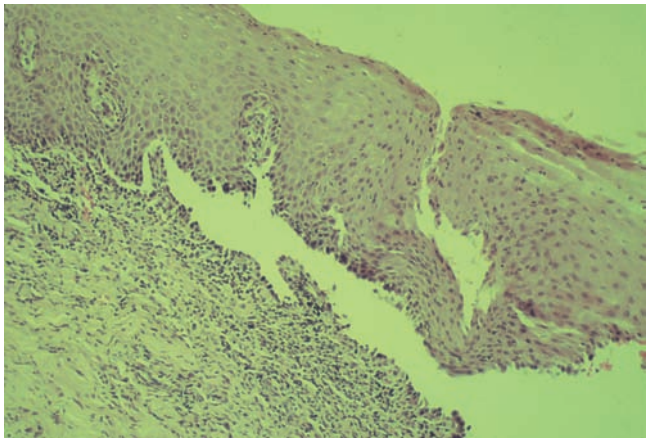

FIGURE 11.16. Histology of oral mucous membrane pemphigoid.

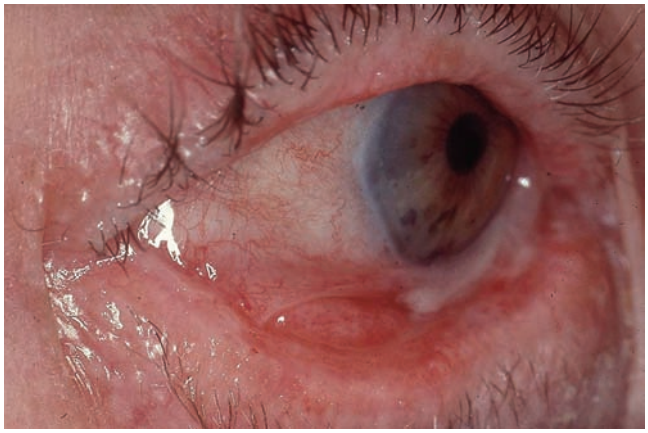

FIGURE 11.18. Ocular mucous membrane pemphigoid (symblepharon). (Courtesy of Dr. T.D. Rees.)

Perioral and Intraoral Characteristics: The oral cavity is the most frequently involved site. Figure 11.17 shows the clinical features of oral MMP, exhibiting erythematous, shiny red gingival tissue. The gingiva is a target site for oral MMP, and localized or generalized desquamative gingivitis is present more than 90% of the time. The gingiva is highly friable (easily crumbles) and even gentle oral hygiene measures or eating may cause the tissue to slough, leaving a painful, erythematous or ulcerated surface.

Distinguishing Characteristics: The lesions are confined to the gingiva in over 50% of cases. A positive Nikolsky sign is usually present. (See Clinical Protocol #3 for maintenance of patients with mucosal disease.) Eye lesions are more common in MMP. Figure 11.18 shows ocular mucous membrane pemphigoid with scarring of the tissues. An eye specialist should evaluate patients. Scarring and **symblepharon,** the adhesion of the inner eyelid tissue to the eyeball, may occur (as depicted in Fig. 11.18).

Significant Microscopic Features: Subbasal layer separation of the epithelium from the underlying connective tissue is characteristic. The separation occurs within the basal lamina, and the inflammatory infiltrate within the connective tissue is nonspecific. Immunofluorescence is positive, revealing a linear pattern of IgG and complement in the basement membrane. This can be drug induced with patients taking medications such as clonidine and penicillamine, but this is true in few cases.

FIGURE 11.17. Oral mucous membrane pemphigoid demonstrating red, shiny gingival tissue. (Courtesy of Dr. T.D. Rees.)

Dental Implications: Not applicable

Differential Diagnosis:

1. Other vesiculobullous diseases need to be considered, including: bullous pemphigoid, pemphigus, erosive lichen planus, erythema multiforme, discoid lupus erythematosus, etc.
2. Generalized desquamative gingivitis is more common in MMP, although localized desquamative gingivitis may be a feature of other vesiculobullous disorders. Extensive skin involvement is rare in MMP in contrast with pemphigus, erythema multiforme, lupus erythematosus, lichen planus, and bullous pemphigoid.
3. Contact allergies may be involved. Generalized erythematous gingivitis is a feature of toothpaste allergy, but bullae formation and classic desquamative gingivitis are rare. Cinnamic aldehyde and other flavoring agents are especially common allergens in oral hygiene products and many foods (see Clinical Protocol #6). Since the flavoring agents are used in so many products, the clinical appearance is becoming more common. Generally, the area of tissue that is exposed to the offending products remains inflamed, and areas of tissue not exposed to the product exhibit clearing. This is true for toothpaste and other flavoring agents that the person is using. Figure 11.19 shows a gingival reaction to cinnamic aldehyde, with reddened tissue and clearing in the oral vestibule.
4. MMP lesions are chronic in contrast with the acute onset associated with erythema multiforme.
5. With any nonhealing, chronic-type condition, there is always the possibility that changes have occurred since the last maintenance visit. The clinician should always

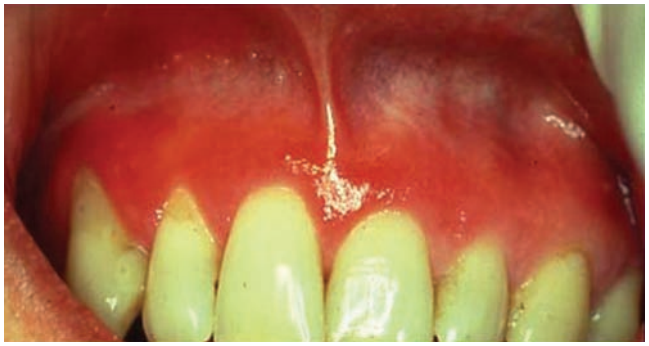

FIGURE 11.19. Cinnamic aldehyde reaction on the gingiva. (Courtesy of Dr. T.D. Rees.)

entertain the possibility that, even though a diagnosis has been made previously, a patient may have a new disease or the existing disease has taken a different course. This is especially true for any mucosal disease that is chronic. Chronic inflammation of the tissues may lead to a more serious state, such as carcinoma. Again, intraoral documentation with the use of photography should be used and is a standard part of monitoring chronic disease states.

Treatment and Prognosis: Often, identifying and discontinuing the offending product is all that is needed. Discontinuing the use of oral products that burn, such as alcohol-based mouthwashes, spicy foods, cinnamon, and strong flavoring agents, is suggested. This will often help lessen the tissue sloughing that causes erosive lesions. Avoiding toothpaste and mouth rinses that contain sodium laurel sulfate is also helpful. Many hidden flavoring agents are present in foods such as salsa, processed foods, and soft drinks such as colas. Canned goods may also have additives that pose a problem for patients with mucosal disease. A dietary analysis should be performed for patients to assist them in avoiding substances that may cause discomfort or worsen the mucosal condition. Patients who are diagnosed with cinnamon allergy usually exhibit normal tissue within a 2-week period.

The use of corticosteroids may predispose patients to candidal infections, and prophylactic prescriptions of an antifungal agent such as nystatin would be considered. (See Clinical Protocols #2 and #5 for diagnosis and treatment.) Individuals afflicted with desquamative gingivitis have difficulty maintaining good oral hygiene and are highly susceptible to dental and/or periodontal disease. Consequently, they should receive frequent maintenance visits, and all treatment procedures should be performed as atraumatically as possible.

NAME: Bullous pemphigoid

Etiology: Bullous pemphigoid is an autoimmune disease.

Epidemiology: Bullous pemphigoid affects a slightly older age group usually in the seventh to eighth decade of life. There is an equal distribution of males and females.

Pathogenesis: The disease is similar to mucous membrane pemphigoid. Bullae are formed because of separation between the basement membrane and the underlying connective tissue.

Perioral and Intraoral Characteristics: Intraoral involvement is relatively rare (10 to 40%). When present, it affects the gingiva. Cutaneous bullae develop slowly and may last for weeks to months before breaking, thereby creating painful erythematous and ulcerative lesions. Oral lesions are similar in appearance to those of mucous membrane pemphigoid. Lesions usually occur on the gingiva, palate, floor of the mouth, tongue, or buccal mucosa. The disease follows a chronic course, although remissions are common. Healing usually occurs without scarring. Unlike mucous membrane pemphigoid, bullous pemphigoid usually affects the skin first.

Significant Microscopic Features: The microscopic features are similar to those of mucous membrane pemphigoid. Figure 11.20 shows a bullous lesion of pemphigoid on the buccal mucosa.

Differential Diagnosis: Microscopic examination and immunofluorescence testing are needed to differentiate this disease from other bullous diseases. The characteristic lack of oral lesions should help separate some cases.

Treatment and Prognosis: Systemic corticosteroids alone or in combination with other immunosuppressive agents are required. Other treatment may include dapsone, cyclosporine, sulfapyridine, and niacinamide. Periodic digital images are helpful in assessing tissue changes in all mucosal diseases (see Clinical Protocol #3). Plaque control is beneficial, with frequent prophylaxis. As discussed above, patients with mucosal disease may have trouble tolerating flavoring agents and abrasive dental products. Alcohol is also an irritant, and alcohol-containing products should be discontinued. Remission is common after 2 to 3 years. However, bullous pemphigoid can be a chronic disorder for some patients. The disease is rarely fatal.

FIGURE 11.20. Bullous pemphigoid. (Courtesy of Dr. T.D. Rees.)

Congenital or Genetic Diseases

Genetic diseases and disorders affect vital organs and tissues during development, resulting in clinically diverse conditions. Factors such as exposure to environmental materials, radiation, infections, certain medications, alcohol, and diseases can contribute to the etiology of congenital disorders. For example, a woman who is exposed to rubella in the first 3 months of pregnancy is at high risk of producing an offspring with birth defects. Additionally, genetic disorders may be inherited as autosomal dominant recessive and X-linked disorders (see Chapter 6). Certain diseases can occur during cell development and division, while other defects may not be obvious until later in life, and the individual may be affected at certain life stages.

NAME: Epidermolysis bullosa

Etiology: **Epidermolysis bullosa** (EB) represents a diverse group of inherited and acquired diseases characterized by fragility of the skin and mucosa, with four main categories recognized (simplex, junctional, dystrophic, and mixed). The molecular basis is not known for 13 different EB conditions. Depending upon the specific type of the disease, individuals will exhibit different levels of severity. EB represents a group of conditions with several subtypes and varying degrees of debilitation with each type. The disorders are related to genetic defects in critical components of the epidermal–dermal border including basal cells, hemidesmosomes, and anchoring connective tissue filaments.

Method of Transmission: EB is a rare group of conditions with both autosomal dominant recessive and X-linked modes of inheritance with over 20 different forms identified. In addition to the genetic forms of these conditions, there is also an acquired autoimmune form known as **epidermolysis acquisita**, which is discussed in the next section.

Epidemiology: Infants are affected with onset at or within a few weeks of birth. The simplex form, which is typically the least severe, may not be recognized initially, with diagnosis generally being made between the ages of 0 and 4 years old. The disease affects both males and females equally. The *National Epidermolysis Bullosa Registry Reports* estimate that approximately 12,500 persons have some form of EB. It is estimated that there are 50 EB cases per 1 million births, with more than 92% of these diagnosed as the simplex form discussed below. The numbers of reported cases vary with each country.

Pathogenesis: There are four major subgroup categories: simplex (typically the mildest form), junctional, dystrophic, and mixed EB (Kindler syndrome). The skin and mucosa exhibit varying degrees of fragility and can blister following mild trauma. The precise pathogenesis varies in the specific defects in the basement membrane area and the level of tissue cleavage after a traumatic incident.

Extraoral Characteristics: All categories feature bullae formation at birth, but the simplex form is the least severe and may improve at puberty. The extraoral manifestations vary markedly between the different EB types and the depth of tissue cleavage. The deeper the cleavage, the greater the likelihood of severe scarring as is often seen in the dystrophic forms. Skin lesions often affect areas of exposure and abrasion such as hands, knees, axilla, and the groin, but all the skin has an increased fragility.

Crusted erosions, milia, pigmentation, and alopecia are commonly seen. Digital webbing with mitten-type deformities of the hands and feet may be seen in the severe dystrophic forms of EB. The varying combinations and types of EB that affect various organs such as the musculoskeletal system, intestinal tract, eyes, and esophagus produce different degrees of affliction. Additionally, anemia is associated with certain EB subtypes due to poor iron absorption and chronic blood loss through large erosive skin lesions. Ocular involvement, particularly corneal, is common in some EB subtypes. Figure 11.21 shows the clinical features of EB.

Perioral and Intraoral Characteristics: Oral lesions can occur in any subgroup, but individuals who require special dental care are usually those with the dystrophic and junctional forms. Their oral erosions can be either mild (usually the dominant form) or severe with scarring (usually the recessive form). Depending upon the type and severity, oral lesions may be occasional blisters with small discrete vesicles that heal rapidly without scarring or they may be more severe ongoing oral lesions with scar formation. Bullae and painful erythematous or ulcerative lesions can be found on any oral mucosal surface. With the more severe EB subtypes of disease, any eating or oral hygiene can cause traumatic insult, resulting in lesion formation. The oral and esophageal involvement with scarring and constriction often seen in the recessive dystropic EB affects eating and swallowing and sometimes makes the passage of food impossible. Many severely affected patients have G-tubes to assist with nutritional intake.

Distinguishing Characteristics: All lesions, whether oral or cutaneous, occur as the result of some trauma and can heal with some scarring (although scarring is most typically seen in most simplex types). Fingernails are often obliterated because of scarring over time. In the severe dystrophic forms, scarring results in ankyloglossia, microstomia, and vestibular obliteration. These oral features can make normal intake of nutrition and clearing food from the oral cavity very difficult.

Significant Microscopic Features: Histopathologic features depend on the genetic abnormality that is present. All forms involve separation of the epithelium from the underlying connective tissue. Blistering occurs within the epidermis (simplex type), within the basement membrane (junctional type), or beneath the basement membrane (dystrophic forms) in inherited EB. In the mixed EB subtype (Kindler syndrome), this separation is variable.

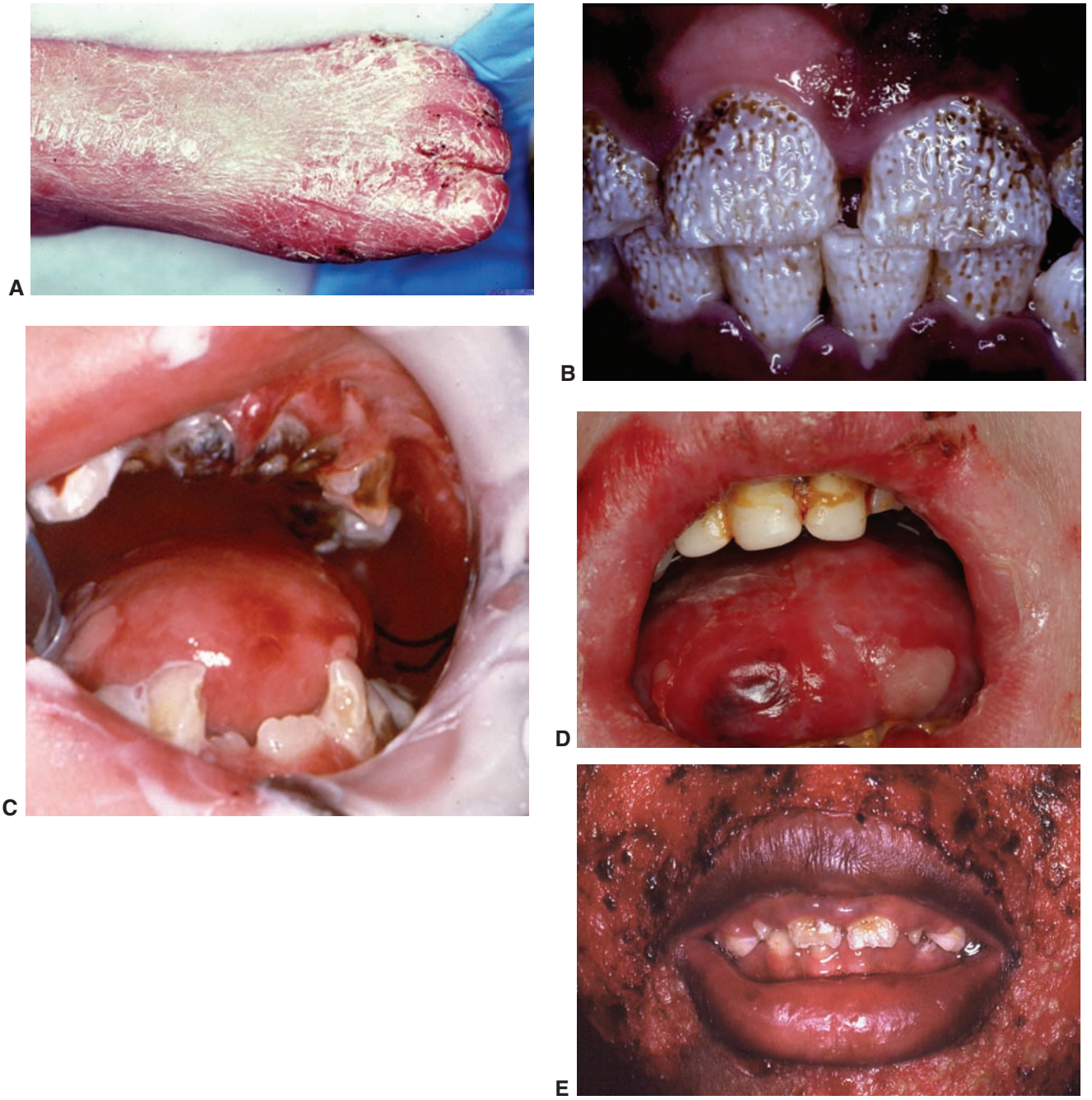

FIGURE 11.21. Epidermolysis bullosa. **A.** Mitten-like scarring of the foot. **B.** Enamel hypoplasia. **C.** Oral lesions of a child **D.** Blistering and scarring. **E.** Oral and perioral scarring. (Courtesy of Dr. J. Timothy J. Wright.)

Dental Implications: Enamel hypoplasia can occur in developing teeth in junctional EB types, and there is a high rate of caries in patients with the junctional and dystrophic forms of EB. The ability of the patient to tolerate a dental procedure depends upon the severity of the EB. Patients who have milder forms of the disease can tolerate normal dental procedures without much difficulty. The patient's tolerance for dental procedures depends upon the degree of EB and the amount of tissue trauma caused by the actual procedure. Patients with milder forms can tolerate in-office procedures with a local anesthetic, while a patient with a more severe form could require hospitalization with general anesthesia, depending upon the extent of treatment needed. Oral hygiene procedures can be modified to accommodate the various types of EB with limited tissue disruption. Specially formulated rinses without alcohol may help with caries control. Systemic use of fluoride, a soft-bristle brush with a small head, and swabbing the medications on without tissue contact or trauma is optimal. Topical fluorides such as increased-strength dentifrices (e.g., 500 ppm), daily sodium fluoride mouth rinses (0.05%), and fluoride varnishes are very helpful in managing the increased risk for caries in junctional and dystrophic EB patients.

Differential Diagnosis: Occurrence of the disease in infancy rules out the other bullous diseases.

1. Late onset dystrophic EB must be differentiated from epidermolysis bullosa acquisita (EBA) (discussed in the next section) by histologic and immunofluorescence studies.
2. Sequencing of the specific causative genes is typically performed to diagnose the different EB subtypes.

Treatment and Prognosis: Wound care for mild cases, antibiotics to prevent secondary infection, and plastic surgery to correct deformities caused by scarring are all treatments for this disease. Dental care requires nonabrasive, nonirritating chemical substances and avoidance of trauma. Promoting a noncariogenic soft diet helps to reduce future caries. In addition, fluoride applications may assist in reducing carious lesions. Patients should be instructed in gentle home care techniques, and antimicrobial mouth rinses may be required (e.g., 0.12% chlorhexidine). Patients with mild forms of the disease can withstand gentle prophylaxis. Scaling and root planning and the successful use of acellular dermal allografts to gain attached gingiva have been described. Successful osseointegration of endosseous implants has also been reported. The prognosis depends on the type of genetic defect and can range from good to fatal.

Epidermolysis Bullosa Acquisita

Epidermolysis bullosa acquisita (EBA) is a chronic blistering disease that can affect the skin and the oral mucosa. EBA is caused by circulating autoantibodies to the dermal–epidermal junction, with two types of EBA: inflammatory and noninflammatory. The antibodies react to a dermal protein that is the constituent of anchoring fibrils and autoantibodies are directed toward type VII collagen. Anchoring fibrils are thought to anchor the epidermis and its underlying basement membrane zone to the papillary dermis. The classic form of EBA is characterized by fragility of the skin including Nikolsky sign, with blisters that coalesce and break open, and vesicles or bullae with localized skin erosions. Lesions heal with milia and scarring. The exposed skin areas such as knees, elbows, nails, feet, and hands are most often the target areas for injury. The disease is rare, affecting approximately 0.2 million people. There is no sex or race predilection.

This unusual autoimmune disease primarily occurs in adults, although it also has been described in children. On occasion, the onset of EBA correlates with development of a variety of underlying systemic diseases and has been associated with systemic lupus erythematosus (SLE), Crohn disease, diabetes mellitus, myasthenia gravis, and rheumatoid arthritis. Other reports correlate the onset with the use of specific medications that are often used in treatment of various disease processes. EBA may have clinical manifestations similar to those of EB, but it can usually be differentiated by the age of onset. EBA features dermal and mucosal bullae formation as found in other blistering diseases. Figure 11.22 shows ulcerations in the lower mucosal region of the lip. Two forms are presented, one inflammatory and one noninflammatory that is the classic type found in most cases. The skin is fragile, with blisters producing vesicles and bullae. The lesions heal but with scarring.

FIGURE 11.22. Epidermolysis bullosa acquisita. A lesion on the lower oral mucosa. (Courtesy of Dr. Michael Brennan.)

Establishing a diagnosis can be difficult. For example, clinical features, histologic findings, and immunofluorescence characteristics of EBA may mimic bullous or mucous membrane pemphigoid. Special immunoelectron microscopy evaluation of biopsied tissue is required if the disease is suspected. Treatment most often consists of the use of systemic corticosteroids and immunosuppressive agents such as methotrexate, azathioprine, or cyclophosphamide. Oral corticosteroids are used to control oral lesions along with specific home care instructions.

Because of the similar name, it should not be confused with EB. Additionally, because of the bullous and vesicle formations when trauma is induced, the hygienist should use caution in scaling procedures since these patients suffer when ultrasonic devices are used at high power. Harsh or abrasive products cause problems as well and air polishers will be highly destructive.

SUMMARY

- Lesions that appear as vesicles can be as innocuous as the mucocele and as extreme and life threatening as pemphigus vulgaris or EB.
- Viral infections such as herpangina, hand-foot-and-mouth disease, and measles all have vesicle formations but are caused by very different viruses.
- Clues such as clinical features, age, sex of the patient, duration of the symptoms, and the location of lesions begin to play a key part in determining the diseases in question. As the clinician assesses the vesicle or combinations of lesions, a pattern of factors begins to emerge in the thought process.
- Further diagnostic testing such as histology, cytology, immunofluorescence, and genetic analysis assists in making a definitive and accurate diagnosis of vesiculobullous lesions.
- The practitioner should be able to account for any lesion in the mouth or any changes that have occurred since a previous visit.

- All lesions have a history, and it is important to account for any tissue change in the mouth by working through the differential process.
- Treatment should be postponed when active herpetic lesions are present.
- Herpetic lesions reoccur and may have prodromal signs prior to the reoccurrence.
- Assisting the patient in containing the spread of herpetic labialis through patient education is crucial.
- Herpes zoster is due to the reactivation of the VZV that is commonly contracted during childhood.
- Childhood vaccines not only limit the spread of infectious diseases such as chickenpox and measles but also eliminate infections such as herpes zoster or shingles that occur later in life.
- Autoimmune diseases, such as pemphigus vulgaris, pemphigoid, and variants of these diseases, may have a vesicle-like appearance.
- Specific care and treatment are indicated for each of the mucosal diseases depending upon the severity of the disease.
- EB is found in four major subgroups: simplex, junctional, dystrophic, and mixed.
- EBA occurs in later life, resulting from the use of specific medications, and correlates with the development of other systemic diseases.
- Precautions for dental treatment must be taken in both autoimmune and genetic-type diseases that exhibit vesicle formations. Tissue trauma should be minimized and abrasive products discontinued.

CHAPTER REVIEW

Case Study 11.1

Your patient is an 18-year-old male who watched the lesion on his lower lip grow larger overnight (Fig. 11.23). He tells you that he was studying, and tried to move a large book from a shelf and pulled too forcefully, hitting his lower lip with the book. The area felt tender and grew in size within hours. The cause of the lesion is probably trauma related to his actions. A biopsy proved the lesion to be a mucus extravasation phenomenon. Answer the following questions:

FIGURE 11.23. (Courtesy of Dr. Brad W. Neville.)

1. If you could view the center of this lesion, which of the following would you expect to find?
   - **a.** Epithelial tissue
   - **b.** Fibrous connective tissue
   - **c.** Saliva
   - **d.** Mucus
   - **e.** Blood
2. If you were to palpate the lesion, what would you expect to find?
   - **a.** A firm consistency
   - **b.** A fixed consistency
   - **c.** A fluid or fluctuating consistency
   - **d.** A papillary consistency
   - **e.** The liquid inside would be released
3. How do you think the patient would describe how the area of the lesion feels?
   - **a.** Painful
   - **b.** Pruritic
   - **c.** A pulsating sensation
   - **d.** Numb
   - **e.** Not painful
4. Damage to which of the following structures would cause the mucocele in the lower lip?
   - **a.** The glands of Blandin-Nuhn
   - **b.** Wharton's duct
   - **c.** Minor salivary accessory ducts
   - **d.** A major salivary duct
   - **e.** The parotid gland
5. Given the clinical appearance of the image presented, which of the following would NOT be considered as very likely in a differential diagnosis?
   - **a.** A vascular lesion
   - **b.** Mucoepidermoid carcinoma
   - **c.** Venous varix
   - **d.** Lipoma
   - **e.** Dermoid cyst

For answers and additional review activities, log in to **thePoint.lww.com**

Case Study 11.2

Study the image of the tongue in Figure 11.24, then answer the following questions:

FIGURE 11.24. (Courtesy of Nancy W. Burkhart, RDH, Ed.D.)

1. Based on the image, would your initial impression be to classify the tissue on the tip of the tongue as inflammatory, developmental, or traumatic? Why would you make this classification?
2. Is the noted tissue change sessile or pedunculated (stalk-like) in appearance?
3. Is the noted tissue change possibly vascular? Why or why not?
4. What would be a good way to evaluate this tissue for a vascular component?
5. Do you think that the tissue change is one that is new or long-term?
6. What would be your opinion of the possible etiology?
7. How do you think this tissue would appear microscopically?

For answers and additional review activities, log in to **thePoint.lww.com**

Critical Thinking Activities

A. How would you differentiate benign mucous pemphigoid (BMP) from toothpaste allergy or an allergic response from a dental product? What factors might lead you toward a toothpaste allergy? Points to consider:

1. Toothpaste allergy presents with a clearing in the vestibule. Why does this occur? Try to imagine how the tissue in the vestibule is somewhat protected by the surrounding tissue.
2. Toothpaste allergy does not produce the denuded, friable consistency of the gingiva that can be observed in BMP or other mucosal diseases.
3. Discontinuing the toothpaste and dental products in question will produce a somewhat rapid response and will diminish lesions within a 2-week period.

B. Mr. Anderson, 52, has been seen in your practice every 4 to 6 months for many years. He usually presents with some generalized erythema of the gingival tissues, but you have always attributed this to his lack of compliance with the recommended 3-month maintenance appointments and poor oral hygiene when he is out of town or busy. He travels frequently and has missed or rescheduled appointments many times. Today, he informs you that he has been told by his family physician that he has ocular pemphigoid. Considering this recent diagnosis, answer the following questions.

1. Describe the type of oral manifestations that might be associated with this type of vesiculobullous disorder.
2. What oral findings in Mr. Anderson's previous dental appointments could be associated with this diagnosis?
3. If Mr. Anderson is exhibiting oral manifestations of pemphigoid, what appointment modifications, if any, would need to be made? What information could you give him regarding management of his disorder at home?

Portfolio Possibilities

- Construct a patient education sheet for patients with pemphigoid and pemphigus. List the facts about the disorders with clear and concise educational information for a newly diagnosed patient. (See the guidelines for Maintenance Appointments in Clinical Protocol #3.) Include dental home care procedures and food products that should be avoided.
- Construct an information sheet for parents of children who may be diagnosed with herpangina, measles, or hand-foot-and-mouth disease. Include phone numbers, contact information, and any pertinent information that a parent may find useful.
- Develop a patient diet diary for 1 week. Have the patient list all brands of foods with the amount consumed. This should include any mints, gum, or beverages that the patient eats for a week. Have the patient bring in the diary, so that you can evaluate the contents. Patients often report more symptoms from their mucosal disease

after consuming certain food products. This could be very helpful in the maintenance program for the individual patient. Include your office logo on a small page-lined book that can be professionally printed. This is not only a great tool for the patient but promotes your office protocol as well.

- The protocol of your practice should be clear to new patients. Your office staff should decide on when a patient should not be seen (unless there is an emergency) and when observed lesions should be biopsied, followed, and evaluated. Consider obvious lesions such as HSV. For example, if the patient has an active lesion, the staff will know that the policy is to give them a reappointment for a later date. Creating a standard information sheet on any shared views, policies, and protocol alerts patients to what standards exist within your practice. Using this sheet when situations arise ensures that everyone will be aware of the proper office protocol and there will be no surprises. This information sheet can also be shared with new patients, so that they know your office policy from their first visit.

Media Menu

Web Sites

American Academy of Oral Medicine
http://www.aaom.com/

Centers for Disease Control and Prevention: Emerging Infectious Diseases Journal
http://www.cdc.gov/ncidod/eid/index.htm

Debra (The Dystrophic Epidermolysis Bullosa Research Association of America)
www.debra.org

The World Health Organization
http://www.who.int/en/

Study Tools

Take advantage of additional online resources to help you study and ace your exams!

- Answers to case studies in the book
- Additional case studies and answers
- Interactive quiz bank with answer feedback
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- Expanded Media Menu with direct links to related Web sites and multimedia resources
- Supplemental references

thePoint Online resources and links are available at http://thepoint.lww.com/DeLong2e

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Chapter 11 **LESION/CONDITION SUMMARY TABLE**

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/INTRAORAL)	MICROSCOPIC/RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Mucocele	Trauma or severance of the salivary duct	Mucin in the duct is blocked at the opening of the duct.	Soft, elevated tissue with a cloudy blue hue Usually under 1.5 cm in size	The collection of mucin is walled off with granulation tissue.	Surgery, removal of the duct and marsupialization	Continued injury to the site when eating/chewing occurs due to excess tissue formation.
Primary Herpetic Gingivostomatitis	Primary infection with the human herpesvirus type 1	Initial exposure to the virus usually in childhood with/without symptoms	Fiery red, marginal gingivitis with small vesicular lesions throughout the mouth and lips	Cells of HSV are seen microscopically as ballooned with microscopic inclusions and multinucleation.	Palliative with soft diet Antipyretics and topical pain relief Antivirals should be given early and appear to decrease viral shedding. Hydration is also important.	Treatment should never proceed because the virus can spread through aerosols, potentially infecting others and making infection worse for the patient by contaminating other areas on the face and around the lip area.
Secondary or Recurrent Herpes Simplex Virus	Reactivation of the initial and latent virus	The cycle of HSV reactivation occurs creating vesicular lesions.	Small coalescing vesicles that rupture and crust When on lips, it is termed herpes labialis.	Tzanck cells are present and acantholytic epithelial cells.	Antiviral agents applied topically Educate the patient on prodromal signs of eruptions and suggest lip balms with SPF protection	Treatment should not proceed when lesions are present and any sign of exudate is noticed.
Herpetic Whitlow	Occurs as a primary infection	HSV occurs on terminal segment of a finger.	Red finger with swelling	HSVs are seen as in the primary infection	Antiviral agents applied topically	HSV can be transferred to other areas of the body such as the mouth, nose, genitals, and eyes.
Ocular Herpes	Occurs through self-inoculation or splash, aerosols, and debris	The virus can occur in any lining mucosa.	Red, painful, draining of the eye	HSV as seen in primary infection	The patient should be under the care of an eye specialist.	The patient should know that herpes may be transferred through autoinoculation to other areas of the body as stated above.
Genital Herpes	May occur through sex or self-inoculation	HSV virus	The genital and oral HSV appear similar clinically.	HSV as seen in primary infection	The patient should be under the care of a physician/specialist.	The patient should know that herpes can be transferred through autoinoculation to other areas of the body.
Primary Varicella–Zoster (chickenpox)	Varicella–zoster virus	Enters through the respiratory tract and carried through the blood stream into the epidermis	Small vesicles that rupture and crust Appears as a rash on the trunk of the body and small vesicles present intraorally	Superficial intraepithelial vesicles	Vaccines are provided and given in combination with MMR vaccines.	Encephalitis and pneumonia can occur. Treatment should not proceed until the patient is disease-free.
Secondary Varicella–Zoster	Caused by latent varicella–zoster virus	Reactivation of the varicella virus initially causing chickenpox	Small vesicles appearing as a rash, but stopping at the midline of the body The virus does not migrate far beyond the area of skin or mucous membrane supplied by the infected nerve.	The same as those seen with the primary form (chickenpox)	Herpes zoster (shingles) may be prevented/lessened by vaccination in those over 60 y of age. Antiviral agents may be administered in the very early stages and may lessen or prevent postherpetic neuralgia. Viral shedding may be reduced.	The patient may seek dental treatment because of initial pain that involves the nerves of the ophthalmic division of the trigeminal nerve causing extreme pain.

continues

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/INTRAORAL)	MICROSCOPIC/RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Hand-foot-and-mouth Disease	A-16 virus and other coxsackievirus A and B strains	Replication of virus in the lymphoid tissue transmitted airborne and oral/fecal routes	Maculopapular rash, soles of feet, palms of hands, and vesicles intraorally	Intraepithelial vesicles precede shallow ulcerations resembling small ulcers.	Treatment is directed toward symptomatic relief. Antipyretic agents and topical medications	Oral lesions cause pain and difficulty with eating and swallowing.
Herpangina	Coxsackie A strains A-16	Enters the body through airborne, fecal route, and easily transmitted in close contact	Rash, oral lesions in posterior of the mouth, soft palate, tonsil region Diffuse reddening with vesicles	Not applicable	Palliative	Dental treatment should not proceed until all vesicles are healed.
Rubeola (measles)	Paramyxoviridae	Arises in winter and spring An incubation period of 10–12 d Spreads through respiratory droplets	Rash, Koplik spots, fever, and malaise	Epithelial cells become necrotic.	Palliative MMR vaccine	In severe cases, pitting of the enamel can occur. Dental treatment should be postponed.
Rubella (German measles)	Togavirus	Arises in the oropharynx and regional lymph nodes, spreads through the blood stream Can cross placenta	Malaise and fever Lymphadenopathy Dark red papules on soft and hard palate Forchheimer sign	Serologic analysis	Palliative vaccination	No dental treatment should occur. There is a risk to pregnant patients who may enter the office.
Pemphigus Vulgaris	Autoimmune	Human leukocyte antigens	Painful, oral lesions, bullae, and ulcers Membranes are erythematous. Nikolsky sign PV may be fatal in some cases.	Acantholysis, Tzanck cells, irregularly arranged basal cells; protein is attacked in the desmosomes.	Steroids—both systemic and topical to control pemphigus vulgaris, careful selection of nonabrasive toothpaste with limited flavoring agents	Careful, low-trauma dental treatment The tissues are highly susceptible to epithelium stripping. Air polishers and abrasive materials should not be used.
Mucous Membrane Pemphigoid (desquamative gingivitis when affecting gingiva) Bullous Pemphigoid (occurs in older adults)	Autoimmune	Antibodies that target the basement membrane	Erythematous tissue, shiny red gingival tissue Highly friable Painful and prone to chronic sloughing	Subbasal separation Inflammatory infiltrate Immunofluorescence needed to confirm IgG and complement at basement membrane	Steroids Careful selection of nonabrasive toothpaste with limited flavoring agents	Careful, low-trauma dental treatment The tissues are highly susceptible to stripping. Air polishers and abrasive materials should not be used. Ocular evaluation should occur with a specialist.
Epidermolysis Bullosa	Congenital/genetic disease—autosomal dominant or recessive	Four major subgroups: simplex, junctional, dystrophic, mixed	Fragility of the skin and mucosa Infants exhibit signs at birth. Painful skin blisters at all skin surfaces May be fatal in some cases	All forms involve the separation of the epithelium for the underlying connective tissue. Blister formation	Antimicrobial oral rinses Wound care with antibiotic coverage, plastic surgery to correct severe deformity	Nonabrasive dental products, non cariogenic diet, gentle home care Scaling and root planing in some cases with acellular dermal allografts to gain attached gingiva
Epidermolysis Bullosa Acquisita	Correlates with underlying systemic diseases Certain medications have been reported to cause EBA.	Dermal and bullous formations	May mimic bullous or mucous membrane pemphigoid	Bullous formation—as with other bullous skin lesions, there is separation of the epithelium and underlying connective tissue.	Systemic and/or topical steroids and immunosuppressants	Careful scaling procedures Gentle debridement Selection of home care products should be nonabrasive and very bland.

CHAPTER 12

Ulcers and Ulcer-Like Lesions

KEY TERMS

Actinomycosis
Adenocarcinoma
Aphthous ulcers
Behçet syndrome
Carcinoma
Chancre
Condylomata lata
Deep fungal infections
Erosive lesions
Erythema multiforme
Erythroleukoplakia
Erythroplakia
Factitial injury
Fibrinous exudate
Gonorrhea
Gumma
Hutchinson triad
Iatrogenic injury
Keratin nests (pearls)
Libman-Sacks endocarditis
Lupus erythematosus
Mucous patches
Mulberry molars
Morsicatio buccarum
Necrotizing sialometaplasia
Necrotizing ulcerative gingivitis
Nonpathogen
PFAPA
Pyostomatitis vegetans
Reiter syndrome
Sarcoma
Speckled erythroleukoplakia
Squamous cell carcinoma
Stomatitis medicamentosa
Stomatitis venenata
Sutton disease
Syphilis
Traumatic ulcer
Ulcer
Urticaria

LEARNING OUTCOMES

1. Define three common ways that a patient may develop a traumatic ulcer.
2. Differentiate and define the key words *factitial* and *iatrogenic*.
3. Describe the clinical characteristics and etiology of necrotizing sialometaplasia.
4. Discuss the confusion that may occur related to malignant lesions and necrotizing sialometaplasia.
5. Define each of the key vocabulary terms for this chapter.
6. Describe the clinical characteristics of the major, minor, and herpetiform types of aphthous ulcers.
7. List the lesions associated with each stage of syphilis.
8. Describe the clinical characteristics of gonorrhea.
9. List the organism involved in gonorrhea and the usual oral site that is commonly seen clinically.
10. List the etiology of the following deep fungal infections: mucormycosis, histoplasmosis, blastomycosis, cryptococcosis, and aspergillosis.
11. Describe the triad of signs and symptoms related to Reiter syndrome.
12. Describe the triad of signs and symptoms related to Behçet syndrome.
13. List the etiology and clinical characteristics of Stevens-Johnson syndrome.
14. List the key clinical characteristics of squamous cell carcinoma (SCC).
15. Define the term "field carcinogenesis."
16. Describe the clinical features of lupus erythematosus.
17. List five characteristics of erythroplakia.
18. What is meant by erythroleukoplakia?
19. List the four most prominent areas of the mouth for oral cancer.
20. List at least four statistical facts related to oral cancer.
21. Describe the clinical characteristics of a hypersensitivity reaction.
22. List the types of erythema multiforme (EM) and the clinical significance of each.
23. Describe the characteristics of Crohn disease and list the clinical signs of the disease as well as the signs of a recurrence.

CHAPTER OUTLINE

Ulcers and Inflammatory Lesions
- Traumatic or Inflammatory Lesions
  - Traumatic ulcers
  - Necrotizing sialometaplasia
- Infectious Agents
  - Syphilis
  - Gonorrhea
  - Actinomycosis
  - Necrotizing ulcerative gingivitis
  - Deep fungal infections
- Immune System Disorders
  - Aphthous ulcers
  - Behçet syndrome
  - Reiter syndrome
  - Erythema multiforme
  - Hypersensitivity reactions
  - Lupus erythematosus
  - Crohn disease
- Neoplasms
  - Squamous cell carcinoma

RELATED CLINICAL PROTOCOLS

#3 Maintenance Appointment Guidelines for the Patient with a Mucosal Disease
#4 Treating Patients with Xerostomia
#8 Treating Patients with Intraoral Ulcers
#11 Patient Education: Oral Cancer Self-Examination
#19 Oral Health Care Management for the Patient with Cancer
#26 Helping Relationships for Dental Hygienists
#27 Motivational Interviewing for Behavior Change
#28 Saliva Testing

Ulcers and Inflammatory Lesions

An erosive lesion may simply be defined as the loss of the epithelial covering of tissue. The lesion may or may not involve pain and will vary in size. Figure 12.1 depicts an aspirin burn producing an ulcer on the tongue and the buccal mucosa. **Erosive lesions** are denuded areas that occur above the basal cell layer of the epithelium. The term **ulcer** is used when the lesion penetrates the epithelium and extends into the dermis. Ulcers often exhibit a red halo or border with a yellow center. The yellow hue is caused by the thin yellow **fibrinous exudate** that covers the ulcer. The process of inflammation causes the ulcer to appear red, which accentuates the yellow hue of the exudates.

Ulcers may have multiple causes, but often they are due to **factitial** injury. This is self-induced injury, and an example would be a traumatic lip bite. Figure 12.2 represents a traumatic ulcer that is factitious—this child bit his lip following anesthesia. Figure 12.3 shows a fingernail injury at the gingivae in a 2-year-old child.

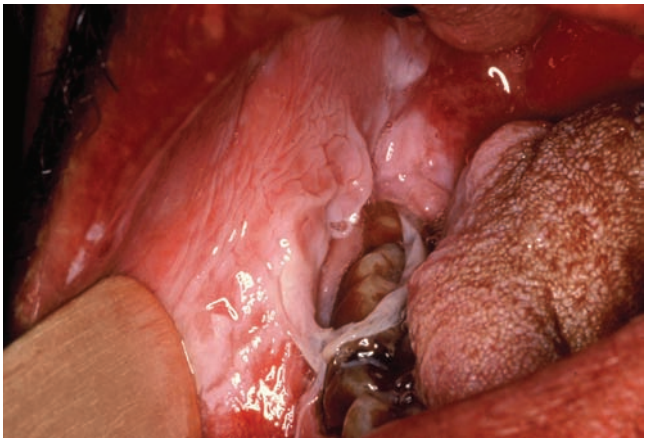

FIGURE 12.1. Chemical burn (aspirin) to the tongue and buccal mucosa. (Courtesy of Dr. Michael Brennan.)

The term **traumatic ulcer** is used to denote an injury to the existing tissue. In some cases, a direct chemical injury such as an aspirin burn may occur. Electrical burns have also been reported as the origin of traumatic ulcers. Ulcers may also be **iatrogenic**. Iatrogenic ulcers are caused by the treatment that is rendered. For instance, the patient may have a dental procedure performed, and trauma from the actual procedure may induce formation of an ulcer. Perhaps a saliva ejector was pressed down on the tissue in the floor of the mouth for too long or with too much pressure, or maybe the patient was injected with anesthesia and an ulcer appeared at the site of the injection. Figure 12.4 shows a traumatic ulcer that is iatrogenic because the tongue was traumatized by an instrument. Figure 12.5 shows a traumatic ulcer caused by multiple carpules of anesthetic injected in the site. Sometimes, an impression is taken, and the tray scrapes or presses the tissue too forcefully, causing an injury. These examples are considered iatrogenic.

FIGURE 12.2. The lip was bitten after being anesthetized. (Courtesy of Dr. Terry Rees.)

FIGURE 12.3. Gingiva has a factitial injury by a young child with a fingernail. (Courtesy of Dr. Terry Rees.)

Systemic problems related to medications, diseases, and malignancy may produce ulcerative lesions. It is often a process of elimination and investigation for the practitioner to determine the source of the lesion, based on a good medical history and a thorough clinical evaluation. In the case of factitial injuries (those produced by the patient), removal of the source of likely trauma is the first step in the tissue healing response. For instance, a sharp edge on a tooth may induce an ulcerative response over a period of time, and smoothing the roughness may provide a quick tissue response, or the patient may traumatize an area by biting a lip that is anesthetized. These ulcers usually resolve when the trauma is removed. However, other ulcer-like lesions that have an immunologic component or a bacterial source will take longer to resolve or may continue to be a chronic problem for the patient. This chapter covers many of the ulcerative lesions that the practitioner sees in clinical practice.

FIGURE 12.4. Traumatic ulcer of the tongue due to handpiece injury. (Courtesy of Dr. Peter Jacobsen.)

FIGURE 12.5. Iatrogenic injury due to multiple carpules of anesthesia. (Courtesy of Dr. Terry Rees.)

Traumatic or Inflammatory Lesions

NAME: Traumatic ulcers

Etiology: Traumatic ulcers may occur at any time and at any location in the mouth. Some patients may traumatize the oral tissue because of improper alignment of the teeth or improper brushing techniques, including brushing aggressively. Dentures that do not fit properly may cause tissue damage, or the patient may traumatize tissue, such as the buccal mucosa or tongue, while chewing.

Method of Transmission: Traumatic ulcers are localized to the area of trauma and are not contagious.

Epidemiology: Traumatic ulcers may occur in any age group, and there is an equal distribution between males and females.

Pathogenesis: External forces are directed toward the tissue causing trauma to the area and subsequently producing the ulcerations.

Extraoral Characteristics: The extraoral characteristics may involve the lip area if traumatized, and this area can appear crusted and sometimes bleeding because of continued trauma.

Perioral and Intraoral Characteristics: Ulcers often have a crater-like appearance with some fibrinous exudate depending upon the degree of trauma.

Distinguishing Characteristics: When repeated trauma occurs, damaging the tissue, the injury may induce scar tissue. The area may be a source of irritation because of the excess tissue and the tendency of continuous injury to the site. Thickened, keratinized tissue in the area of injury often causes the tissue to appear white and may indicate some type of frictional injury to the tissue. An example would be the chronic "cheek chewer," with the technical name of **morsicatio buccarum.**

Significant Microscopic Features: The microscopic findings are nonspecific and not diagnostic, exhibiting an inflammatory process with a loss of the epithelium. Figure 12.6 depicts the histology of an ulcer. The epithelium has been lost in one area of the lesion, and the ulcer is covered by a fibrinous exudate with underlying granulation tissue in the same area. A heavy infiltrate of lymphocytes is present.

Dental Implications: Continued trauma may occur because of more injury to the tissue. Discomfort may be present, and dental work should be postponed until a later date and until the lesions have completely healed. If another injury does not occur in the same region, the traumatic ulcer eventually heals. Scar tissue may form in severely traumatized tissue, and the person may easily traumatize the same area again.

Differential Diagnosis: Any ulcerative condition must be considered. Traumatic ulcers may be confused with the following:

1. Ulcers produced by microorganisms, such as those involved with tuberculosis, discussed in Chapter 10
2. Syphilis, discussed in this chapter
3. Gonorrhea, discussed in this chapter
4. Aphthous ulcers, discussed in this chapter

Treatment and Prognosis: Discomfort is usually mild, although in some cases eating may be difficult. The ulcers are usually short-lived and resolve with no problems other than mild discomfort to the patient. Removing the source of injury should allow recovery of the tissue. Of course, any lesion that does not heal within 2 weeks or one in which no possible etiology is found should be evaluated further.

NAME: Necrotizing sialometaplasia

Etiology: The entity originates from salivary gland ischemia that causes necrosis of the tissue, usually due to trauma in the local area. This may be from trauma due to previous surgery or possibly from previous local anesthesia administered in the site. Local blood supply to the area is disrupted, causing ischemia.

Method of Transmission: Necrotizing sialometaplasia is not contagious; it is localized and self-limiting.

Epidemiology: All ages are equally affected, and necrotizing sialometaplasia occurs equally in males and females.

Pathogenesis: **Necrotizing sialometaplasia** is a benign entity that occurs at the juncture of the soft and hard palate, producing disruption of the tissue at this site. Although the lesion is not malignant, it may be confused with malignancies such as mucoepidermoid carcinoma. A careful evaluation and biopsy are needed to produce a definitive diagnosis; however, the lesion will usually heal without complications. Figure 12.7 depicts the palate region with necrotizing sialometaplasia.

External Characteristics: Not applicable

Perioral and Intraoral Characteristics: The tissue may appear as an elevated mass that subsequently becomes ulcerative.

Distinguishing Characteristics: A deep demarcated ulcer is characteristic of necrotizing sialometaplasia. The deep lesion subsequently becomes coated with a thick yellow fibrinous covering.

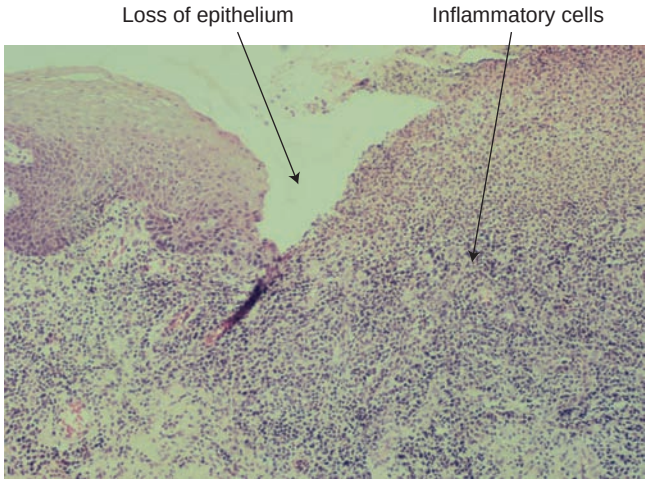

FIGURE 12.6. Histology of an ulcer.

FIGURE 12.7. Necrotizing sialometaplasia in the palate region. (Courtesy of Dr. Michael Brennan.)

Significant Microscopic Features: Necrosis of the salivary gland is involved, and there is squamous metaplasia of the salivary duct epithelium. Necrotizing sialometaplasia may resemble malignancies in both clinical and microscopic appearance.

Dental Implications: The correct diagnosis is essential to ensure patients are not subjected to unnecessary surgery.

Differential Diagnosis: Considerations would be the following:

1. Syphilitic gummas, discussed later in this chapter
2. Mucoepidermoid carcinoma—Chapter 17
3. Deep fungal infections, discussed later in this chapter
4. Salivary gland neoplasms—Chapter 17
5. SCC should be considered. Due to the histologic pattern, necrotizing sialometaplasia is sometimes confused with SCC. SCC is discussed throughout the book.

Treatment and Prognosis: Analgesics may be recommended. There is no surgical intervention, and a biopsy should be taken to confirm the diagnosis. The prognosis is excellent, and healing occurs after several weeks to months.

Infectious Agents

Microorganisms surround us, but most do not cause disease in the host because of the unique properties of the immune system. The natural barriers that provide defense, such as the skin and mucosal surfaces, surround us and help defend us (see Chapters 3 and 4). Some microorganisms cause disease (pathogens), and many are considered non–disease causing **(nonpathogenic).** Since standard precautions are taken with each patient, the distinction is not an issue in the clinic. The following section focuses on the distinction of common oral disorders that arise from various microorganisms and manifest as oral ulcers or erosions. The chapter is related to the clinical features and treatment of each disorder.

NAME: Syphilis

Etiology: **Syphilis** is caused by the spirochete *Treponema pallidum* through direct contact with the primary lesion.

Method of Transmission: Syphilis is spread through venereal transmission from sexual contact, from mother to fetus, or by the transfusion of infected blood. Transmission occurs during oral, anal, or vaginal sex. The organism dies quickly on dry surfaces and when exposed to air. This organism is not transmitted through toilet seats, hot tubs, eating utensils, or other casual contact. A previously infected individual may contract syphilis again and become infected again if exposed to the spirochete.

Epidemiology: Since 1900, the overall number of syphilis cases has declined, with the exception of a sharp increase during the 1940s and a peak in 1980. The peak in 1980 coincides with an increase in the number of AIDS cases, both primarily due to a surge in unprotected sex. A sharp 90% decline occurred from 1990 to 2000. In 2004, the overall incidence was 7,353 cases. The South continued to have the highest rates of any region in the United States at 3.6 per 100,000 individuals (CDC & P, 2005 National Report). According to the Centers for Disease Control and Prevention (CDC), there were 12,401 to 13,066 cases of early latent syphilis reported in the United States in 2009 for men aged 20 to 24 years old (CDC updates, 2011). Recent updates (2012) note increases in congenital syphilis, with a total of 33 states reporting one or more cases of congenital syphilis. The increase in syphilis of women is the cited reason. The disease is more prevalent in black men and patients with AIDS and less frequent in Native Americans. There is also a higher rate with men who have sex with men (CDC, 2009). Mortality from syphilis occurs in approximately 20% of untreated patients and is most likely due to complications of late disease. In January 2011, the CDC brought together clinicians treating patients with sexually transmitted diseases to further discuss the guidelines set in 2010 for treatment. Both recognition and treatment options are important in containing the spread of syphilis. The CDC requires physicians to report chlamydia, gonorrhea, and syphilis. These three represent only a portion of sexually transmitted diseases in the United States.

Pathogenesis: Syphilis is transmitted through sexual contact and is classified as a sexually transmitted disease. Although syphilis has persisted for decades, its increase over the last couple of decades is of specific concern. Syphilis is spread through sexual contact through breaks in the skin because of genital ulcers that can bleed easily. During sex, delicate tissues in the rectal, vaginal, and oral linings and in the external genitalia allow penetration of the bacterium. Without treatment, syphilis progresses through three stages: primary, secondary, and tertiary. There is also a period of latency after the secondary stage that can last for years only to recur as the tertiary stage when the proper treatment has not been given. The infection can also be spread from the mother to her fetus as discussed previously.

Extraoral Characteristics: The features differ depending upon the stage of disease. Skin lesions can be apparent on the extremities. Syphilis lesions appear on the genitals, involving the penis, vulva, and anus. Later-stage syphilis that has not been treated can involve the eyes, causing blindness.

Perioral and Intraoral Characteristics: Syphilis may have various oral appearances that depend on the stage of infection in the individual. Three prime stages occur:

- Primary stage: After direct contact with an infected individual, the person develops a **chancre.** Figure 12.8 shows an ulcerative lesion on the lower lip at the site where the spirochete entered the host. The lesion typically appears within 1 week to 3 months after contact. This usually occurs on the penis, vulva, anus, or mouth. This chancre will heal within several weeks with no other signs of the disease. The most common site for oral lesions is on the

FIGURE 12.8. Chancre on the lip from syphilis. (From Smeltzer SC, Bare BG. Textbook of medical-surgical nursing. 9th ed. Philadelphia: Lippincott Williams & Wilkins, 2000.)

lip, but they may be seen on the tongue, tonsils, or other mucosal areas. The lesions are painless and may appear as a firm, indurated lesion with an ulcer-like appearance that rapidly becomes eroded. Lesions at this stage are highly infective, and a diagnosis followed by treatment is crucial.

- Secondary stage: Several weeks after the primary stage, the host develops a secondary stage that manifests with flu-like symptoms, fever, swollen lymph nodes that are nontender, skin lesions, and some mucocutaneous lesions. The lesions associated with this stage are called **mucous patches.** Figure 12.9 depicts a mucous patch on the mucosa near the vermilion border of the lip. The patches may be ulcer-like, with a pseudomembranous covering exhibiting yellow, white, or gray coloring. The highly infectious lesions of syphilis are teeming with organisms. During this stage, the practitioner may notice papillary lesions known as **condylomata lata**, and there may be a rash on the trunk of the infected person. The rash may be on body parts such as the face, palms, feet, trunk, etc. The saliva is highly infective during this stage (see Chapter 16).

FIGURE 12.9. Mucous patch on the lip from syphilis. (Courtesy of Dr. E. J. Burkes.)

BOX 12.1

The Stages of Syphilis

Stages of Syphilis	Dental Implications
Primary incubation: 12 to 30 days	Chancre—Usually occurs on genitals but can occur orally Lymphadenopathy Patchy alopecia
Latent	The disease appears dormant. This latent stage can occur between the secondary and tertiary stage as well.
Secondary	Mucous patch Bilateral cutaneous rash Condylomata lata
Latent	The disease appears dormant. This latent stage can occur between the primary and secondary stage as well. This stage can exist for decades.
Tertiary	Gumma seen orally Syphilis affects the cardiovascular system and the CNS. Altered mental state
Congenital	Hutchinson triad 1. Mulberry molars and notched incisors 2. Inflammation of the cornea 3. Eighth nerve deafness Additional nasal deformity and excessive bone growth may occur—frontal bossing.

- Tertiary stage: The third stage produces some serious complications that affect multiple organs. A **gumma** may appear initially as an indurated mass and, subsequently, an ulceration that promotes extensive tissue destruction in the localized area of the gumma. Gummas can appear on the face and extremities as well as the genitals. Most frequently, the palate and the tongue are involved. The palatal lesion may be extensive enough to penetrate to the nasal cavity. Gummatous syphilis may affect the skin, bone, and mucous membranes, and the lesions often cause local destruction of the affected organ system. During the late stages of syphilis, paralysis, insanity, blindness, knee joint damage, personality changes, impotency, aneurysm, and tumor on the skin or internal organs may occur.

In congenital syphilis (Box 12.1), the organism that infects the mother is passed on to the developing fetus, resulting in numerous clinical malformations. Pregnant women infected with syphilis have a high risk of having a stillborn baby. Babies born to infected mothers need to be treated immediately after birth.

Distinguishing Characteristics: As discussed above, some subtle clinical manifestations may go unnoticed or be mistaken for other oral conditions or ulcer-like lesions. With congenital exposure, the teeth are affected, resulting in the molar teeth exhibiting rounded, berry-shaped elevations on the occlusal surfaces, and they are known as **mulberry**

molars. The incisors have a notched appearance due to the spirochetes infecting the enamel organ during the formation of **Hutchinson incisors**. The described effects on the teeth are part of a triad of occurrences, called **Hutchinson triad,** that also include deafness due to the loss of function of the eighth cranial nerve and opacification of the cornea with loss of eyesight. See Chapter 21 for a clinical representation of the Hutchinson triad.

Significant Microscopic Features: Specific stains in a dark-field examination of a smear are used to view the numerous "corkscrew-like" organisms that are diagnostically significant in extraoral syphilis. Specific blood tests are used such as the VDRL and the RPR tests. Results of these tests are positive throughout the first two stages. Serologic tests are also used, which include the fluorescent treponemal antibody absorption tests and the *T. pallidum* hemagglutination assays (TPHA). The FTA-ABS is used as a check against test results, and the specific diagnostic tool that is used is determined by the existing stage of the disease.

Dental Implications: Specific to dentistry is what is known as Hutchinson triad, which involves three factors: (1) inflammation of the cornea, (2) eighth nerve deafness, and (3) dental abnormalities. The abnormalities are related to congenital exposure of the child resulting in the molar teeth being formed with a rounded, cup-shaped appearance and the incisors developing a notched appearance due to the spirochetes infecting the enamel organ during formation. The person who has been exposed may present with external skin lesions, and in some instances, there may be visible evidence of lesions around the periphery of the lip.

Differential Diagnosis: Since the incidence of syphilis is low, it is sometimes unnoticed and undiagnosed when seen clinically. Syphilis is termed "the great imitator" and rightfully deserves its name because of the multiple clinical manifestations that the disease presents. If oral lesions are not present or are very subtle, the disease could go unnoticed. The ulcer-like lesions make syphilis easily confused with other diseases. The clinician may want to consider the following diseases in a clinical diagnosis:

1. Necrotizing sialometaplasia—Chapter 12
2. Aphthous ulcers—Chapter 12
3. Mucoepidermoid carcinoma—Chapter 17
4. Tuberculosis—Chapter 10
5. Squamous cell carcinoma—Chapter 12
6. Trauma—Chapter 12

Treatment and Prognosis: The standard treatment is penicillin. The outcome of treatment will depend upon the stage of the disease and the amount of the damage that has occurred. The tertiary stage may last for years, and severe damage to organs may have occurred if prior treatment was not initiated. Sometimes, the patient does not seek treatment for the symptoms of syphilis, and the subtle signs may go unnoticed, placing the patient and those in contact with the person at high risk.

NAME: Gonorrhea

Etiology: **Gonorrhea** is sexually transmitted and, when treated, can be cured. The bacterium *Neisseria gonorrhoeae,* the gonococcus, infects the genital tract, mouth, and rectum of both men and women.

Method of Transmission: Gonorrhea is transmitted through sexual contact and can be transmitted from mother to child across the placenta and during birth in the birth canal. The oral lesions of gonorrhea result from oral–genital contact. Babies may be infected in the birth canal.

Epidemiology: In 2010, some 309,341 cases of gonorrhea were reported to the CDC. Approximately 62 million new cases of gonorrhea are reported each year internationally (WHO). In the United States, the CDC estimates that 700,000 people are infected with new cases each year. Approximately 75% of all reported cases of gonorrhea are found in people aged 15 to 29 years. The highest rates of infection are usually found in 15- to 19-year-old women and 20- to 24-year-old men. The disease is sexually transmitted. The rate is higher in homosexuals and prostitutes than in the general population. More than a million cases are reported annually in the United States, and this number has risen in the last few years. The incubation period is approximately 7 days, but symptoms may be present 1 to 14 days after the initial infection. Gonorrhea is a common cause of pelvic inflammatory disease (PID) in women, with about 750,000 cases reported yearly.

Pathogenesis: Gonorrhea is caused by the organism *N. gonorrhoeae*, the gonococcus. It is spread by direct contact with the penis, vagina, mouth, or anus of an infected person. The disease produces inflammation of the reproductive and urinary tracts in the form of urethritis in men and vaginal discharge with inflammation of the cervix in women. In women, the opening to the uterus, the cervix, is the first place of infection. The disease can spread into the uterus and fallopian tubes, resulting in PID, which can cause tubal (ectopic) pregnancy and infertility in as many as 10% of infected women. The disease is mentioned here because oral signs may be present, and although the disease is not common, reported cases have increased in the past few years. Since many cases are not reported, the numbers may be much larger than those documented, according to the CDC.

Extraoral Characteristics: The person may appear in poor health and exhibit lymphadenopathy (swollen lymph nodes).

Perioral and Intraoral Characteristics: The most common site is the oral pharynx, with resultant gonococcal pharyngitis. The tonsillar region is often affected, with inflammation and pustular lesions. Figure 12.10 shows the oropharynx with the tissue appearing red and swollen. Figure 12.11 shows a heavy coating on the tongue and other tongue lesions associated with gonorrhea. Other common complaints may

FIGURE 12.10. Oral gonorrhea. (Courtesy of Dr. Michael Krakow.)

include halitosis, stinging, and burning. Generalized stomatitis may be seen in some cases.

Distinguishing Characteristics: The presenting features are not diagnostic, and other factors need to be considered such as lifestyle and health history. As noted in the presentation of syphilis, gonorrhea may have a varied clinical appearance.

Significant Microscopic Features: Gram stains and serologic tests are used to make a definitive diagnosis. When left untreated, the inflammatory response becomes chronic, with macrophages and lymphocytes predominant.

Dental Implications: When oral lesions are observed, the oropharyngeal areas are the most vulnerable. Because of the usual oral–genital practice involved and the associated trauma to the tissues, the pharyngeal tissues may appear ulcerative and erythematic. Ulcerative lesions may also be observed.

Differential Diagnosis: Other ulcerative conditions should be considered such as the following:

1. Aphthous ulcers—Chapter 12
2. Herpetic lesions—Chapter 11

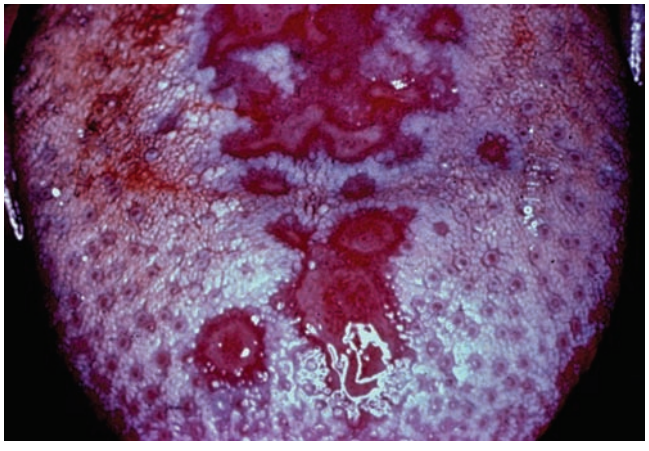

FIGURE 12.11. Oral gonorrhea. (Courtesy of Dr. Michael Krakow.)

3. Pemphigus and other mucosal diseases—Chapter 11
4. Cancer of the tonsil—Chapter 12

Treatment and Prognosis: Antibiotic therapy is used with combinations of antibiotics, depending on the region of the world. Drug-resistant strains have become more common, and the CDC recommends a combination of drugs. They also recommend that the person be tested for other sexually transmitted diseases (STDs) as well. Additionally, hepatitis C may be a concern for these individuals. Commonly, the following antibiotics are the drugs of choice and given in a single dose with a combination of antibiotics: cefixime, ceftriaxone, and doxycycline or azithromycin. For oropharyngeal treatment, ceftriaxone plus azithromycin or doxycycline is typically given. Alternatives are given if there is an existing allergy. This infection results in blindness in some countries where antibiotics are not routinely administered at birth into the conjunctiva. The prognosis is good if discovered early. Urethral stricture is a common complication.

NAME: Actinomycosis

Actinomycosis is a chronic bacterial disease that manifests in the formation of an abscess, sometimes draining externally. The lesion is often observed during the extraoral examination as a draining lesion in the lower facial region.

Etiology: Actinomycosis is caused by *Actinomyces israelii*, an anaerobic or microaerophilic, gram-positive bacterium usually associated with initial tissue trauma. The name of this disease is confusing, since the mycosis suffix would lead one to categorize the name with fungal infections; however, actinomycosis is a bacterial infection. Since these gram-positive bacteria are components of the normal flora, they work in conjunction with other bacteria in the mouth and are kept in check.

Method of Transmission: Since actinomycosis is considered a bacterial infection, it is not a contagious disease. Actinomycosis develops in cases related to trauma such as from surgery, tooth extraction, root canals, tonsil crypts, and carious lesions. These factors predispose the individual to its invasion through mucosal tears and openings, thereby positioning the person for the subsequent development and progression of the bacteria.

Epidemiology: Any age group may be affected, but actinomycosis occurs predominately in adults. The infection occurs in both males and females.

Pathogenesis: The primary characteristic of actinomycosis is the abscess formation and the subsequent draining **fistula**. The bacteria do not exist free in nature but are normal inhabitants of the gastrointestinal tract and the oral cavity. The infections have been reported in patients with AIDS.

Extraoral Characteristics: When actinomycosis occurs in the oral region, it may become an indurated, ulcerative lesion developing into a fistula leading out through the skin of the neck or mandible. The extreme exudates that build

FIGURE 12.12. Draining fistula of the mandible. (Courtesy of Dr. Michael Brennan.)

up eventually develop a tract leading outside of the body. Figure 12.12 shows a draining fistula. Figure 12.13 shows actinomycosis deep within the tissue.

Perioral and Intraoral Characteristics: The site of the lesion is usually ulcerative and may have exudate associated with the ulcer, depending upon the extent of the infection. In the case of extraction sites, the infection would be at the point of the extracted tooth.

Distinguishing Characteristics: The exudate produced is a yellow pus-like substance containing what is known as sulfur granules. This is seen seeping from the fistula and is a clinical clue to actinomycosis.

Significant Microscopic Features: The sulfur granules and the organism are identified through clinical examination, evaluated microscopically, and diagnosed with cultures.

Dental Implications: Other systemic disease states may be present as well, such as AIDS, which has been reported in conjunction with actinomycosis. Often, because of its subtle nature, the more serious disease, such as AIDS, goes unrecognized and is not associated with the occurrence of actinomycosis.

FIGURE 12.13. Deep fungal infections. (Courtesy of Dr. John Jacoway.)

Differential Diagnosis: Considerations should be given to the following:

1. Osteomyelitis—Chapter 20
2. Other bacterial and fungal organisms—Chapter 12
3. Staphylococcus infections may be considered as well—Chapter 23
4. Human immunodeficiency virus (HIV)—Chapter 22

Treatment and Prognosis: The prognosis is good upon dissolution of the infection. High-dose penicillin for extensive periods is the required treatment.

NAME: Necrotizing ulcerative gingivitis

Necrotizing ulcerative gingivitis (NUG) is also formally known as acute necrotizing ulcerative gingivitis. The older term "trench mouth" was given to soldiers during WWII who were diagnosed with NUG. NUG is superimposed on gingivitis or periodontitis (Wilkins, 2012).

Etiology: NUG is an infectious disease primarily of the gingiva, causing gingival bleeding, gingival ulceration, tissue necrosis, and pain. The condition is usually found in young adults. Factors such as stress, lower resistance to disease, poor nutrition, and poor oral hygiene contribute to the disease and predispose the person to the complications of other organisms. The term trench mouth, used for WWII soldiers, evolved because of an inability to maintain adequate oral hygiene along with the living conditions and stress factors that accompany the situations of war. Any of a number of different oral spirochetes is associated with NUG. Organisms such as *Prevotella intermedia*, α-hemolytic streptococci, *Actinomyces* species, *Selenomonas*, *Porphyromonas gingivalis*, *Treponema*, and *Fusobacterium* species are commonly found in NUG.

Method of Transmission: The person has been predisposed by general systemic problems, stress, improper nutrition, and poor oral hygiene practices. Since NUG is an infectious disease, care should be taken to minimize aerosol production during dental procedures.

Epidemiology: NUG is usually found in young adults between the ages of 15 and 30 years, and it is preceded by chronic gingivitis. The NUG is superimposed on gingivitis/periodontitis and usually begins with ulceration and necrosis in the col area. Immunocompromised patients and those receiving chemotherapy may be more susceptible to developing NUG (see Chapter 22 for clinical representation and its relationship to AIDS). An inability to perform adequate home care is also observed in certain disorders such as Down syndrome, making NUG more likely in these individuals. Smoking is a known predisposing factor as well, since tobacco chemicals affect the tissues. There is an equal distribution of males and females.

Pathogenesis: NUG has also been known as Vincent infection because of the description of the lesions in the tonsil and pharynx region by Vincent. The name originates from the spirochete *Borrelia vincentii*, with which it is associated.

However, the term Vincent angina is used incorrectly as a synonym for NUG.

Extraoral Characteristics: The extraoral characteristics may involve the general physical health of the person along with observable characteristics of fever, pain, and swollen lymph nodes.

Perioral and Intraoral Characteristics: NUG presents with sudden, painful swelling of the free gingiva and necrosis with craters in the interdental papillae (see Chapter 22 on AIDS for clinical representation). A fiery red gingiva with bleeding is common. A fetid odor is present, and the patient may complain of a metallic taste. The inflammation may extend into the palatal region and the oral pharynx. A clinical slide of NUG is depicted in Chapter 22 (see Figs. 22.14 and 22.15).

Distinguishing Characteristics: The fetid odor associated with NUG is a factor in distinguishing the disease from other mucosal disorders. A gray pseudomembrane forms over the necrotic gingiva in NUG and spontaneous bleeding occurs with any tissue manipulation. The pseudomembrane is composed of the necrotic tissue, fibrin, microorganisms, and leukocytes (Wilkins, 2012).

Significant Microscopic Features: A mixed flora of spirochetes (*Treponema* spp.), fusobacterium, *Prevotella intermedia*, *Veillonella* spp., and streptococci has been implicated in the disease.

Dental Implications: Debridement of the teeth and affected soft tissue areas is the recommended treatment, along with a proper diet, rest, and stress reduction. Mouth rinses are sometimes recommended to aid in healing (see Clinical Protocol #3). Instruction in brushing and flossing techniques will help the patient maintain a disease-free state. An oral irrigating device should not be used, since microorganisms can be forced down into the deeper tissues and could produce bacteremia. No ultrasonic devices should be used so that aerosol production is minimized, since NUG is an infectious disease. Encourage the patient to continue treatment because the infection may recur if treatment is prematurely discontinued. The use of saltwater rinses, mixtures of peroxide 3% with equal water, or chlorhexidine 0.12% twice daily is suggested (Wilkins, 2012).

Differential Diagnosis: The following disease states may be considered in a differential diagnosis:

1. There is a strong connection with HIV and AIDS—Chapter 22
2. Confusion may occur with other gingival diseases—Chapter 11
3. Herpes simplex infection—Chapter 11
4. The severity of the condition and early clinical similarities may cause confusion with other mucosal conditions—Chapter 11

Treatment and Prognosis: The prognosis is excellent once the infection is treated and oral hygiene is maintained. However, the papillae do not return to normal and suffer the damage of the infection.

NAME: Deep fungal infections

Etiology: Fungal infections may arise from soil, bird and bat droppings, or decaying vegetation. Some fungi reside as normal inhabitants on the body, causing problems only when they are able to enter the body through tears or cuts in the skin. The spores or organisms follow specific routes such as the mucous membranes, which allow the organism to enter the body. For instance, the specific organism involved with histoplasmosis is *Histoplasma capsulatum var. capsulatum*, which enters the body through the lungs.

Method of Transmission: Box 12.2, **Deep Fungal Infections,** shows the specific route of transmission for various organisms. The organisms involved in deep fungal infections inhabit the soil and are found in the natural environment. Some of the organisms are native to certain geographic locations. For instance, according to the CDC 2012 report, histoplasmosis is especially prevalent in the Ohio and the Mississippi River valleys in the United States, Central and

BOX 12.2

Deep Fungal Infections

Disease	Organism	Entry/Source	Clinical Appearance
Histoplasmosis	*H. capsulatum*	Lungs/bat and bird droppings	Indurated ulcers with rolled borders
Zygomycosis (also called mucormycosis and phycomycosis)	*Absidia, Mucor*	Oral/normal inhabitant	Palatal ulceration with fistulas/necrosis
Aspergillosis	*Aspergillus*	Lungs/soil, water, decaying vegetation	Large necrotic ulcers covered by black coat
Cryptococcosis	*Cryptococcus neoformans*	Lungs/prevalent in patients with AIDS	Nonhealing nodules
Blastomycosis	*B. dermatitidis*	Lungs/immunocompromised patients	Irregular ulcerations with firm borders
Coccidioidomycosis	*Coccidioides immitis*	Lungs/desert region soil	Large ulcerations

South America, Africa, India, and Southeast Asia. In most cases, these geographic locations are known to have the *H. capsulatum* organism. Additionally, of HIV-infected persons in these areas, 10 to 25% develop histoplasmosis. The fungal infections continue to increase in proportion to the number of HIV-infected patients, transplant patients, diabetic patients, patients with emphysema, cancer patients, and others who are immunosuppressed (see Chapter 22).

Epidemiology: Every age group may be affected by fungal infections if the host resistance is lowered. There is equal susceptibility, depending on the immune defenses of the person. Elderly patients and those who are immunocompromised are at greater risks.

Pathogenesis: Deep fungal infections occur in the internal organs and the submucosal connective tissue. The tissue in the mouth is very vulnerable to tears, scrapes, and normal trauma. This poses a problem for the person who has an immunocompromised state or a lowered state of health and thus a lowered resistance to pathogens and other organisms. Although the diagnosis of such organisms and lesions cannot be made clinically and requires other tests, the clinician should be aware of the possibilities. Delayed treatment for the patient could make the problem worse.

Extraoral Characteristics: The lesions are usually ulcerative, sometimes necrotic depending on the stage, and they are pseudomembranous.

Perioral and Intraoral Characteristics: Some of the specific fungal infections produce an ulcerative lesion with indurated lesions. These fungal infections have some oral manifestations and warrant consideration in a differential diagnosis. Although rare and usually seen in patients who are debilitated, they may be the first clue to the dental hygienist that there may be a more serious disease entity.

Distinguishing Characteristics: The lesions related to fungal infections may mimic other disease states, and they may be in combination with other health conditions. Some chronic infections may persist for long periods.

Significant Microscopic Features: The organism involved is observed through special cultures and staining procedures. Further culture tests would be performed to confirm the diagnosis.

Figure 12.14 depicts a stained slide of aspergillosis.

Dental Implications: The correct diagnosis is important to establish a treatment protocol. A referral to the correct facility is important if it is determined that the ulcers may be symptoms of other serious disease states. Identification of the organism is important in successfully treating the lesion or referring the patient for further treatment, depending on the type of lesion involved. Box 12.2 provides some well-known fungal infections that would warrant consideration.

Differential Diagnosis: Many of the fungal infections mimic lesions such as the following:

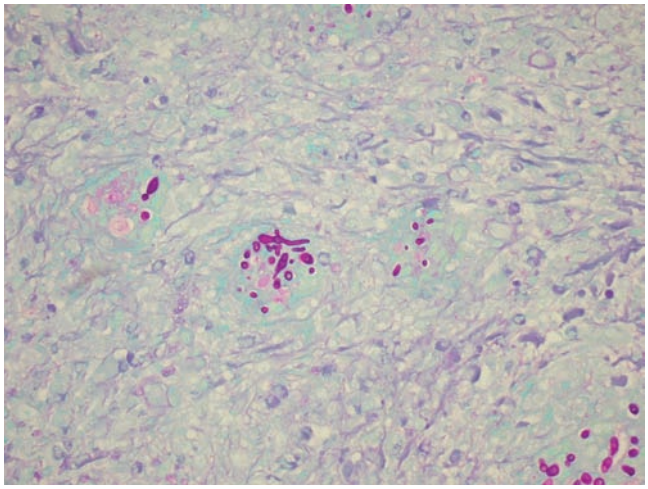

FIGURE 12.14. Histology of aspergillosis. (Courtesy of Dr. Lisa Chang.)

1. SCC—Chapters 5, 12, 14, and 23
2. Mucoepidermoid carcinoma—Chapter 17
3. Ulcerative conditions such as major aphthae, as well as systemic conditions producing ulcer-like lesions—Chapter 12

Treatment and Prognosis: The treatment of choice depends upon the organism. Specific medications are prescribed such as antimicrobial agents including amphotericin B, ketoconazole, and itraconazole. The progress and recovery depends on the particular organism and the ability of the host to render defenses. Patients who have fungal infections may have lung involvement; therefore, a pulmonologist, who specializes in lung diseases, would treat this disease.

Immune System Disorders

The function of the immune system is discussed in Chapter 4, with details of the functions in which the body defends itself against disease and pathogens. During evolution, the human body has acquired ways in which we defend ourselves from natural predators such as animals, environmental conditions, and organisms. These organisms include pathogens such as viruses, bacteria, parasites, and fungi. Some organisms such as those found in the human intestine actually work in a symbiotic-type relationship. Viruses, which are pathogens, do not assist in our survival and are detrimental to our health. The body's natural defenses against microorganisms function in two ways: (1) natural immunity and (2) acquired immunity (see Chapter 4). The diseases listed in this section have oral manifestations and involve the immune system.

NAME: Aphthous ulcers

Etiology: The etiology of **aphthous ulcers** is not fully understood, although some factors associated with aphthous ulcers are stress, trauma, food allergies, genetic predispositions, B_{12} vitamin deficiencies, iron, folate, zinc deficiencies, and hormonal fluctuations. There is also speculation that the initiation is caused by a hypersensitivity reaction,

autoimmune response, and trauma, with chemical mediators involved. Hypersensitivity reactions to sodium lauryl sulfate have been implicated, as well as reactions to medications such as cardiovascular drugs, interferon, certain antibiotics, and anti-inflammatory drugs. Patients with disease states such as Crohn disease, celiac disease, ulcerative colitis, Behçet syndrome, and HIV infection have a high rate of aphthous ulcers as an ongoing part of the disease state (Neceskas et al., 2010).

Three types of recurrent aphthous ulcers (RAUs) are classified as: (1) RAU minor, (2) RAU major, and (3) the herpetiform RAU (not to be confused with the herpes lesions caused by the herpes simplex virus [HSV]) (see Box 12.3). The classification is determined by the size of the lesion and the dispersion. The aphthous ulcer is believed to have an immunologic etiology.

Method of Transmission: Aphthous ulcers are not contagious, in contrast to the herpetic-type lesions, which are spread from person to person and to other parts of the body on the same person.

Epidemiology: Local factors such as trauma are sometimes involved and may be caused by biting the tissue, consuming hot liquids, dental procedures, or dental hygiene procedures that disrupt the tissues. Aphthous ulcers often begin in childhood and decrease with age. Rivera-Hidalgo et al. (2004) analyzed the data (as part of NHANES III) from 17,235 adults, reporting a higher annual prevalence in whites, Mexican Americans, and individuals 17 to 39 years old who were nonsmokers. Blacks were reported to have lower rates of aphthous ulcers. Studies by Tollerud et al. (1991) reported that smoking raises the number of T-helper lymphocytes in whites and lowers it in blacks. Rivera-Hidalgo et al. point out that this may relate to the ethnic differences in why some populations may be more prone to aphthous ulcers. The prevalence in the under 40-year-old age group was almost double that for those over 40 years of age. Aphthous ulcers have been reported to decrease during pregnancy and increase significantly during stressful events. Females reportedly have a higher rate of occurrence, especially in association with the menstrual cycle and hormonal fluctuations (Scully & Porter, 2008).

Pathogenesis: RAUs, also known as canker sores, aphthous stomatitis, or periadenitis mucosa necrotica recurrens, are the most commonly seen ulcerations in the oral cavity. RAUs appear on unkeratinized tissue such as the buccal mucosa, vestibule, the labial mucosa, the ventral surface of the tongue, the oropharynx, and the floor of the mouth. Additionally, the soft palate and the posterior oropharynx may be involved. The herpetic types (HSV) of lesions appear on keratinized tissue and are preceded by vesicles. They are referred to as cold sores by many people. The aphthous form of ulcers also has a distinct size, shape, and location. The lesions are reported to occur more frequently in nontobacco users. This may be due to the effect tobacco has on the mucosa, making it more keratinized and thereby lowering the susceptibility to the ulcers. There is some indication that a substance in nicotine may also play a role in decreasing susceptibility, since patients on nicotine replacement therapy appear to avoid outbreaks. The reported incidence of aphthous ulcers ranges widely, from 5 to 66% of the population.

Ulcerations that appear aphthous-like have also been reported in disorders such as Sweet syndrome, agranulocytosis, cyclic neutropenia, periodic fever syndrome, Crohn disease, Reiter syndrome, Behçet syndrome, systemic lupus erythematosus, celiac sprue (caused by gluten sensitivity), ulcerative colitis, and allergies in general.

BOX 12.3

The Three Categories of RAUs

- RAU Minor. Minor aphthous ulcers may also be called Mikulicz aphthae in some literature. This is the most common of the three types, making up approximately 70 to 87% of all forms of RAUs. Those afflicted are usually aware of a prodromal stage in which they report a tingling or burning sensation. The macule usually develops within 24 to 48 hours and lasts from 7 to 10 days and up to 14 days in some cases. The ulcer will heal without scar formation. Pain may accompany the lesions for several days, and the crater-like ulcer will develop a fibrinous membrane cover appearing white or yellow. The ulcers are surrounded by an erythematous halo. Lesions usually number from one to five and are less than 1 cm in diameter (Figs. 12.15 and 12.16).
- RAU Major. This form has the largest lesions of the three types. Sometimes referred to as **Sutton disease**, or periadenitis mucosa necrotica recurrens, it is much less common in occurrence. Statistics report that from 7 to 20% of RAUs are classified in this variety. The lesions are much larger, ranging from 1 to 3 cm in diameter and usually number from 1 to 10. They also appear deeper and more crater-like and have an irregular border. Because of the extensive lesions and the depth, there is scarring of the tissue and resolution may take up to 6 weeks. Dysphagia and fever are common with the major type of aphthae. Onset of these is usually at puberty. The patient may suffer with the chronic disease for 25 years or

FIGURE 12.15. RAU minor. (Courtesy of Dr. Terry Rees.)

BOX **12.3** **The Three Categories of RAUs *(Continued)***

more (Fig. 12.17). Ulcers are seen in patients with HIV/AIDS that appear similar to major aphthae because of their state of health.

- RAU Herpetiform. These are the smaller of the ulcers, measuring approximately 1 to 3 mm in diameter. They tend to appear in cluster formation of anywhere from 10 to 100 at any time and are painful. This form tends to be more predominant in women and occur later in life. The ulcers may coalesce to produce a wide area of lesion. From 7 to 10% (some authors believe this occurs much less frequently) of all cases of aphthous ulcers are of this type. The herpetiform name is not to be confused with the herpetic-type gingivostomatitis lesions found in the primary form of herpes simplex that may occur in children (see Chapter 11). RAU herpetiform is similar in that the vesicles are small and cluster-like, but RAU herpetiform is found usually on nonkeratinized tissue, and as shown in Figure 12.18, the lesions are found on the ventral surface of the tongue and the floor of the mouth. In contrast, herpetic stomatitis HSV is located on the keratinized tissue of the dorsum of the tongue, preceded by vesicles (Fig. 12.19). The confusion with the herpetic aphthae form is that it can also occur on keratinized tissue as well (just as primary herpetic gingivostomatitis can occur). HSV infection is most commonly mistaken clinically for RAUs.

FIGURE 12.16. RAU minor. (Courtesy of Dr. Terry Rees.)

FIGURE 12.18. RAU herpetiform. (Courtesy of Dr. Marco Carrozzo.)

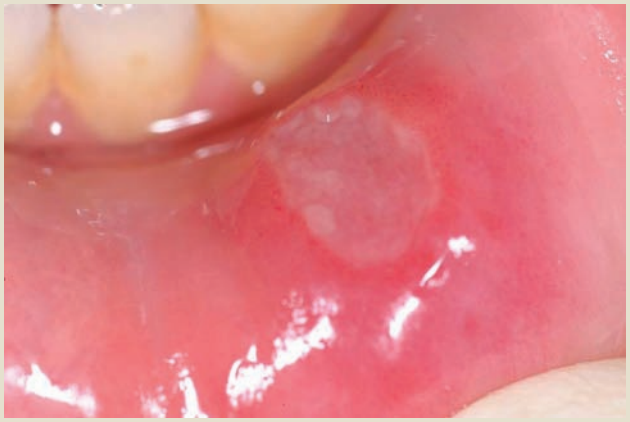

FIGURE 12.17. RAU major. (Courtesy of Dr. Michael Lewis.)

FIGURE 12.19. Herpes simplex virus. (Courtesy of Dr. Peter Jacobsen.)

Extraoral Characteristics: There are no extraoral characteristics related to RAUs unless the lesion is close to the lip and produces edema in that area. The general health and condition of the patient may appear below normal because of pain or fever. Fever is not a noted characteristic; in most cases, it is unusual, but it may be evident in some individuals. Syndromes such as periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis, or **PFAPA**, (Marshall et al., 1989) may be a consideration if a fever does occur. Other possible trigger mechanisms are allergic or hypersensitivity reactions. Additionally, gastrointestinal-related problems, such as Crohn disease or sprue (gluten sensitivity), are considerations. Further, if the aphthous ulcer is large or has been present for a few days, a secondary infection may produce a systemic infection involving the lymph nodes, and a low-grade fever may be produced.

Perioral and Intraoral Characteristics: The appearance and location are important in the clinical diagnosis of all ulcer-type lesions. The ulcer appears as a shallow and somewhat crater-like lesion with a yellow-to-white pseudomembrane and an erythematous border described as a halo appearance.

Distinguishing Characteristics: RAUs are found on nonkeratinized tissue. They are not found on the dorsum of the tongue, the attached gingiva, and the hard palate mucosa that are keratinized. This is in contrast to the herpetic lesions that are on attached, keratinized mucosa. However, with the herpetic form of acute herpetic gingivostomatitis, the lesions may be in both attached and movable mucosa (see Chapter 11). Aphthous ulcers must be differentiated from trauma ulcerations and from other systemic problems that may cause ulcers.

Significant Microscopic Features: There are nonspecific findings, and biopsies are usually not needed. The normal findings are lymphocytes, macrophages, and mast cells. Generally, the biopsy specimen is nonspecific, with just an inflammatory composition.

Dental Implications: Pain may make dental procedures difficult. Patients who are susceptible to RAU may have lesions due to tissue trauma. Multiple visits may be difficult for dental procedures that require additional appointments. Repairing any sharp teeth or restorations reduce the incidence of trauma. Plaque removal and increasing lubrication of the mouth are beneficial to decrease the bacterial counts and inflammation in the mouth (see Chapter 22 for the occurrence of aphthous ulcers in relation to AIDS).

Differential Diagnosis: Some viral infections such as herpangina, gingivostomatitis, and hand-foot-and-mouth disease are part of the differential diagnosis but can usually be eliminated clinically. Some diseases should be considered initially, such as the following:

1. Erythema multiforme—Chapter 23
2. Lichen planus—Chapters 13 and 14
3. Mucous membrane pemphigoid—Chapter 11
4. Pemphigus vulgaris—Chapter 11
5. AIDS/HIV infection—Chapter 22
6. Reiter syndrome—Chapter 12
7. Behçet syndrome—Chapter 12
8. Sprue—Chapter 12
9. Crohn disease—Chapter 12
10. Sutton disease—Chapter 12
11. Systemic lupus erythematosus—Chapter 12
12. PFAPA syndrome—Chapter 12

Treatment and Prognosis: The use of chlorhexidine gluconate as a rinse is often prescribed to patients. Sometimes, topically applied corticosteroid gels such as Kenalog in Orabase are used, depending on the severity and type of ulcerations (see Clinical Protocol #8). Additionally, tetracycline rinses are sometimes prescribed in addition to corticosteroids. Corticosteroids and over-the-counter medications are sometimes suggested when the patient determines that the first prodromal signs have appeared. For severe problems, further testing and screening may be needed. Depending on the number and severity, the lesions usually subside within 7 to 10 days regardless of treatment. In the major forms, the lesions may remain ulcerative for weeks and eventually heal with evidence of scarring. Patients should be encouraged to keep a diary and search for "triggers" that increase the possibility of developing the ulcers. Foods such as nuts, chocolates, acidic foods, citrus spices, and alcohol have been linked to the development of ulcers. Some patients also have high sensitivity to some dental products such as flavoring agents and sodium lauryl sulfate.

NAME: Behçet syndrome

Etiology: **Behçet syndrome** is an inflammatory disorder of unknown cause. A viral connection is suspected, with a genetic predisposition.

Method of Transmission: Behçet syndrome is of an unknown origin, but there is no indication of possible transmission from one person to another.

Epidemiology: Behçet syndrome has an onset in the third and fourth decades. It typically affects persons of

APPLICATION 12.1

Patients often call us or come in for an appointment after a lesion, vesicle, or ulcer has healed. They give us their history of what happened and how long it lasted, usually ending with "I wish you could have seen it!" We are then faced with trying to determine what might have occurred and trying to discern whether the description is anything that produces a medical or dental concern. With the use of cell phones, digital cameras, and the Internet, and with the improvement of the cameras on the actual phones, the opportunity for documentation of these ulcers/vesicles is right at the patient's fingertips. The clinician should tell the patient to take an image of what is occurring and bring in the phone or camera for viewing. For offices that utilize/answer e-mails for patients, it can be sent to the office. Sometimes, patients may not think of this initially, so a friendly suggestion can be helpful the next time something occurs with the patient. If your office sends out newsletters, this is an item that could be mentioned and will be well received by patients. This makes your practice up-to-date and expresses concern for the patient.

FIGURE 12.20. Behçet syndrome.

Mediterranean, Middle Eastern, and Japanese descent. In most geographic areas, men are affected more often the women, except in western countries, where women are affected more than men. Oral lesions are found in over 90% of cases in all types of the disease. Generally, major aphthae are common, with herpetiform being more rare. Both oral and genital ulcers are found in 65% of Behçet patients, and about 80% develop eye lesions as well.

Pathogenesis: The disorder is a rare multisystem disorder noted for a triad of (1) RAU minor, (2) genital ulcers, and (3) ocular lesions. The three factors are required for diagnostic consideration. Other problems related to gastrointestinal, vascular, muscular, and hematologic abnormalities may exist also. Skin lesions including Behçet's are an immune-mediated process leading to vasculitis. Genetic predisposition is suspected, and a viral etiology has been proposed (Fig. 12.20).

Extraoral Characteristics: Cutaneous lesions may be present such as erythema nodosum or acneform skin eruptions, arthritis, central nervous system (CNS) lesions, and intestinal ulcerations (Messadi & Younai, 2010).

Perioral and Intraoral Characteristics: The ulcerative appearance in Behçet syndrome is very similar to the aphthous ulcer. The lesions may range in size from several millimeters to several centimeters. The lesions are recurrent and painful.

Distinguishing Characteristics: The triad of minor ulcers, genital ulcers, and ocular lesions signals the possibility of Behçet syndrome for a disease consideration. When seen with cutaneous involvement and other symptoms, the characteristics become even more pronounced.

Significant Microscopic Features: Enhanced polymorphonuclear leukocyte chemotaxis and neutrophil/platelet hyperfunction. Vasculitis and perivascular infiltrate ultimately develops.

Dental Implications: Medications used in treatment, such as cyclosporine, may produce gingival hyperplasia, and other medications may have effects on the tissue as well. Corticosteroids and immunosuppressive agents often produce changes in the tissues, and the patient should be evaluated with each visit. Maintenance can be adjusted for the individual patient as needed.

Differential Diagnosis: Behçet syndrome may be confused with other disorders that also have oral ulcerations, such as the following:

1. HIV-associated aphthous—Chapter 22
2. Confusion may also exist between RAUs and HSV, especially with regard to the herpetiform types—Chapters 11, 12, and 22
3. Crohn disease—Chapter 12
4. Reiter syndrome—Chapter 12
5. Lupus—Chapter 12

Treatment and Prognosis: Topical steroid treatment may be used. Cyclosporine has been shown effective in the treatment of mucocutaneous and ocular lesions. Chlorambucil may be combined with corticosteroids. The lesions can be controlled but recur frequently in most instances.

NAME: Reiter syndrome

Etiology: **Reiter syndrome** usually develops after exposure to a venereal disease or a gastrointestinal infection, such as dysentery, and is caused by organisms such as *Salmonella* and *Shigella* (Yates & Stetz, 2006). Males who carry the HLA-B27 gene are at risk for Reiter syndrome, which suggests a genetic influence to the disease (Neville et al., 1995; Regezi et al., 2003). Infectious organisms are suspected to be etiologic agents such as *Chlamydia* or *Mycoplasma* spp.

Method of Transmission: Since the syndrome is related to an abnormal immune response, it is not considered contagious. However, an association with HIV-infected individuals has been suggested, and this aspect should be kept under consideration for diagnosis.

Epidemiology: Reiter syndrome usually affects white males of around 30 years of age. Males are affected most often, but females may be affected as well. Although Reiter syndrome has been reported in children, the cases are infrequent. There are no known racial differences.

Pathogenesis: As in Behçet syndrome, this syndrome also comprises a triad of arthritis, urethritis, and conjunctivitis (or iritis, which is inflammation of the iris) (see Fig. 12.22).

Extraoral Characteristics: The small joints of the patient are affected, which usually involve the lower extremities. The genitals, anus, and rectum may be affected. Thickened hyperkeratotic nodules that resemble pustular psoriasis are characteristic. Conjunctivitis is a component of the triad for Reiter syndrome and occurs early in the disease. Dystrophic nail lesions may also be a dermatologic

FIGURE 12.21. Reiter syndrome. (Courtesy of Dr. Terry Rees.)

FIGURE 12.22. Reiter syndrome with ocular inflammation. (Courtesy of Dr. Denis Lynch.)

component. Musculoskeletal problems of the large weight-bearing joints and the ankles are frequently involved and may exhibit redness and swelling. The Achilles tendon may be involved, producing tendinitis. The ocular involvement may include cataracts and glaucoma. The eye appears red and swollen in some cases.

Perioral and Intraoral Characteristics: In the mouth, approximately one-half of patients have oral ulcerations. They appear sharply demarcated, and a white border often surrounds the lesion (Fig. 12.21). Additionally, some of the lesions may appear aphthous-like. Unlike the painful aphthous ulcers, lesions related to Reiter syndrome are often described as less painful. These lesions may occur anywhere in the mouth.

Distinguishing Characteristics: Reiter syndrome may appear similar to other disease states with common findings such as geographic-like tongue, aphthous ulcers, arthritis, and conjunctivitis (Fig 12.22).

Significant Microscopic Features: The lesions resemble psoriasis, with parakeratosis and microabscess formation.

Dental Implications: Assisting the patient in diagnosis of the early disease is important, since the oral signs can mimic other less serious diseases such as common aphthous ulcers. When external symptoms are present along with the intraoral lesions, referral to a medical doctor is indicated.

Differential Diagnosis: The lesions may appear as aphthous-like lesions or geographic tongue, with some lesions appearing as erythematous plaques.

1. Aphthous ulcers—Chapter 12
2. Behçet syndrome—Chapter 12
3. Celiac sprue—Chapter 12
4. Crohn disease—Chapter 12
5. Lupus—Chapter 12

Treatment and Prognosis: Nonsteroidal anti-inflammatory agents are the medications of choice. The disease may last from weeks to months, and the condition can be chronic with remission and recurrence. In most patients, Reiter syndrome usually remits within a year, but in 15 to 20% of cases, progressive arthritis develops.

NAME: Erythema multiforme

Etiology: **Erythema multiforme (EM)** has been associated with exposure to the HSV, tuberculosis, and histoplasmosis, as well as other fungal organisms. Mycoplasma pneumonia and HSV infection are often observed within the previous weeks of skin lesion development (Rubin, 2012). The use of certain medications is also associated with EM, including sulfonamides, penicillin, barbiturates, phenylbutazone, and phenytoin. Sometimes, the cause of the disease is never discovered. As the name implies, the disease can have multiple clinical appearances and forms.

Method of Transmission: Not applicable

Epidemiology: EM affects young adults, and men develop the disease more often than women do. Approximately 25 to 50% of patients who have cutaneous lesions also have oral lesions. The disease can be chronic or may only be seen in an acute form (Plemons et al., 1999).

Pathogenesis: EM is an acute mucocutaneous disease that occurs in two forms. EM minor features distinct skin lesions that are termed "target lesions" or "iris lesions" (Fig. 12.23). The lesions resemble a target or the iris of the eye, with a circular pattern. This form may or may not have oral involvement. EM major is characterized by both cutaneous lesions and intraoral involvement. This second, more severe form is also referred to as **Stevens-Johnson syndrome.** The oral cavity, conjunctiva, and genitalia are involved, and a mortality rate of 5 to 15% is reported (Porth, 2004).

Extraoral Characteristics: The skin lesions present as erythematous papules that enlarge to form central vesicles, or bulla, creating what are referred to as "iris," "target," or "bull's eye" lesions.

Perioral and Intraoral Characteristics: Oral, genital, and ocular lesions may be present, depending upon the type and

FIGURE 12.23. Erythema multiforme target lesions. (Courtesy of Dr. Peter Jacobsen.)

severity of the disease. The lesions may be bordered by a blanched halo with an erythematous zone at the periphery. Ocular lesions may vary in severity when present. Often, the lips are involved and may be covered by a black hemorrhagic crust; the mucosal lesions are raw and red in appearance. Figure 12.24 demonstrates the hemorrhagic state of Stevens-Johnson syndrome in a child.

The oral ulcers may vary from a few aphthous lesions to a large number when the disease is in a major form.

Distinguishing Characteristics: The cutaneous target lesions that are initially seen are the most characteristic sign of EM. The lesions appear as concentric rings with a lighter outer edge and a deeper colored core. The major form of EM is known as Stevens-Johnson syndrome, and this form is often triggered by medications, resulting in a heavy crusting of the lips, which become swollen and hemorrhagic. Figure 12.24 depicts the oral tissue lesions in a patient diagnosed with EM due to a reaction to penicillin.

Significant Microscopic Features: Histologic findings include epithelial hyperplasia, spongiosis, vesicles, and lymphocytic infiltrate. Necrotic keratinocytes and extensive vesicular changes are seen on histologic diagnosis.

FIGURE 12.24. Stevens-Johnson syndrome. A 7-year-old with crusting of the lips due to penicillin reaction. (Courtesy of Dr. John Jacoway.)

Dental Implications: Dental work may exacerbate the disease and must be postponed until the lesions have completely healed.

Differential Diagnosis: Confusion sometimes occurs with the following disease states:

1. Herpes simplex virus—Chapter 11
2. Primary herpetic gingivostomatitis—Chapter 11
3. Other dermatological disorders such as pityriasis, erosive oral lichen planus, benign mucous membrane pemphigoid, and pemphigus vulgaris—Chapter 11

Treatment and Prognosis: Treatment is usually palliative, but short-term. Corticosteroids are used in more extreme cases as well as antiviral medications. The lesions usually subside within a few weeks, but recurrent lesions are possible in about 25% of cases.

NAME: Hypersensitivity reactions

Etiology: **Hypersensitivity reactions** may be caused by new or previously used personal hygiene products (toothpaste, mouth rinses, soaps, and makeup), dental appliances constructed with metals or plastics, household products (chemicals and cleansers), and others. Foods and new or previously taken medications may also cause a localized or systemic hypersensitivity reaction.

Method of Transmission: Individuals may have an inherited predisposition for hypersensitivity reactions.

Epidemiology: Any age may be affected, and an equal distribution of males and females has been reported. With exposure to more chemicals than in previous decades, the numbers of hypersensitivity reactions have increased and are expected to continue to rise.

Pathogenesis: The majority of oral hypersensitivity reactions are type IV delayed hypersensitivity reactions mediated by sensitized T lymphocytes (see Chapter 4). Oral type IV reactions usually take the form of a contact stomatitis or **stomatitis venenata** (the mucosal counterpart of contact dermatitis). This hypersensitivity response is initiated in the tissues contacting the offending substance, causing erythema, ulcers, and possibly swelling. Reactions usually occur within 24 to 48 hours after contact but may occur at any time during or after use. Contact hypersensitivity usually occurs rapidly and resolves quickly, but it may become chronic and the cause may not be easily identified in some patients (see Clinical Protocols #6 and #13). Hypersensitivity reactions caused by systemic medications such as penicillin or sulfa drugs are called fixed drug reactions or **stomatitis medicamentosa**. These reactions can be type I, II, or III and cause signs and symptoms in the oral cavity, such as ulcers and vesicles, as well as skin rashes and lymphadenopathy. EM, which is caused by a response to a systemic medication, is a good example of a type II fixed drug reaction. Oral hypersensitivity reactions may manifest with differing degrees of

APPLICATION 12.2

The dental profession is seeing a surge in the number of patients who present with varying oral symptoms related to hypersensitivity. Most professionals attempt to solve the mystery through trial and error by discontinuing dental products, foods, and other materials (e.g., soaps, detergents, cosmetics, drinks, environmental allergens) that their patients contact daily. Many clinicians, however, do not consider the possibility that intolerance or hypersensitivity could be the sole contributor to the patient's problem with regard to oral symptoms. Stomatology Centers are specialty clinics that treat many such patients who come to the centers because their particular oral condition could not be diagnosed elsewhere. These patients may have seen several other medical and dental practitioners before being referred to a specialty clinic. A reason for the tissue response is usually found, and many times, a hypersensitivity response is the diagnosis. This response may be categorized further into other subclassifications such as contact allergy, cinnamon allergy, toothpaste allergy, or metal allergy.

We are bombarded with so many chemicals and products daily that it is believed that the increase we are clinically observing is related to allergy/hypersensitivity reactions. The possibility that a generalized lip irritation, tissue sloughing, or gingival irritation may be linked to a hypersensitivity reaction is a viable consideration that clinicians should prudently include in their differential diagnosis. Read Clinical Protocol #6 for a checklist of possible flavoring agents and protocols that may be considered.

systemic involvement, local involvement, or both occurring simultaneously.

Extraoral Characteristics: Hives are common in severe allergic reactions. The cutaneous lesions can vary in size, and pruritus may accompany the lesions. Figure 12.25 is an example of hives in an allergic response (type I hypersensitivity) to a shaving skin product.

Perioral and Intraoral Characteristics: Vesicles, erythematous tissue, rash with various sized macules, and ulcers may be seen depending upon the type of reaction and the person's immune system. Cinnamic aldehyde allergy is an example of allergic contact stomatitis caused by cinnamon flavoring agents (cinnamic aldehyde or cinnamon oil) found in chewing gums, toothpastes, mouth rinses, and other foods. When oral tissues are bathed in the antigenic substance as they would be when using cinnamon-flavored toothpaste, for example, a generalized erythematic appearance occurs (Fig. 12.26). Often the area of the vestibule is protected because of overlapping tissues. An area of "clearing" may be observed where the product did not come into contact with the tissues. Cinnamon products as well as other flavoring agents are being used more extensively today, and more cases of this type of allergic reaction are being documented (see Clinical Protocol #6). Restorative materials, such as amalgam, are frequently the cause of hypersensitivity reactions. In a susceptible individual, contact with these materials often causes a lichenoid-type reaction. Rees (2011) states that all metals are capable of releasing metallic ions in the oral environments and the majority of ions reside in the soft and hard tissues that directly contact the restoration or appliance. Further, materials such as nickel, mercury, gold, palladium, cobalt, and platinum have been noted as hypersensitivity reactants (antigens). Various dental product hypersensitivity is a frequent problem for patients, causing redness, irritation, and possibly sloughing of the tissue. Figure 12.27 depicts the sloughing of tissue common in patients experiencing a toothpaste allergy.

FIGURE 12.25. Hypersensitivity reaction. (Courtesy: Dr. Nancy W. Burkhart.)

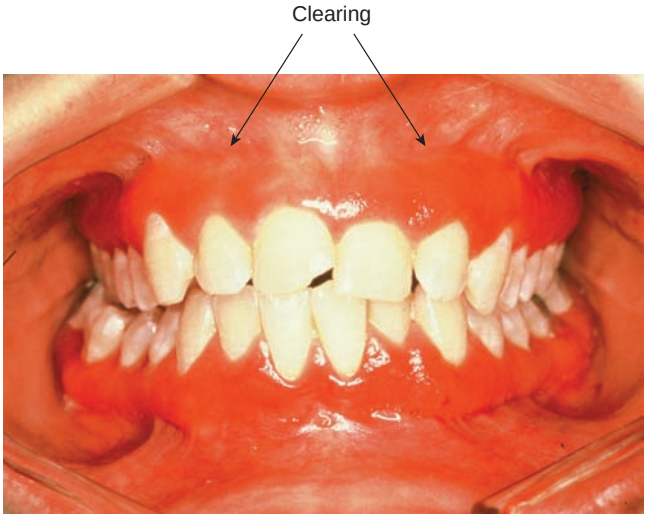

FIGURE 12.26. Toothpaste allergy—cinnamic aldehyde. (Courtesy of Dr. Terry Rees.)

FIGURE 12.27. Tissue sloughing due to sensitivity reaction. (Courtesy of Dr. Terry Rees.)

Distinguishing Characteristics: Type IV hypersensitivity reactions often involve aphthous ulcers and erythema. Often the tongue and the buccal mucosa are the prime areas that are involved.

Significant Microscopic Features: Nonspecific features are seen, such as spongiosis (collections of neutrophils surrounded by clear spaces or halos), apoptotic keratinocytes, lymphoid infiltrates, eosinophils, and ulceration. In addition, mononuclear or polymorphonuclear infiltrations in a subepithelial or perivascular infiltration, basal cell destruction, edema, and keratinocyte necrosis are represented.

Dental Implications: Patients who have hypersensitivity may be predisposed to react to products or chemicals used in the dental office. Rees (2011) states materials such as epoxy, acrylates, and resins have been found to contain over 40 known allergens that can cause hypersensitivity and a chemical irritation in some individuals. Lichenoid reactions are often the result of the exposure, with no clear indication of a true etiology. Other examples of an environmental hypersensitivity exposure include latex allergy (see Chapter 4) and flavoring agents that are found in prophy paste, toothpaste, mouth rinses, and even fluoride. Certain restorative products may produce a response in some patients. When obvious allergy-related problems continue after discontinuing the offending products, it will be necessary to refer the patient to someone for a more extensive evaluation of the condition. A skin prick test or a patch test may be used to determine specific products that the patient is not tolerating well.

Differential Diagnosis: A careful health history is crucial, with emphasis on the current use of medications that may be contributing to the reactions. The oral membranes may be affected or there may be more systemic problems and symptoms. Intolerance or an allergy may occur at anytime during life. The following items should be considered: certain foods, cosmetic and oral products, and many household products. Patients may appear with many ulcerative-type lesions that may clinically appear as the following:

1. RAU—Chapter 12
2. Cinnamic aldehyde reaction—Chapters 11 and 13
3. Lichen planus—Chapters 13 and 14
4. Pemphigus—Chapter 11
5. Pemphigoid—Chapter 11
6. Lupus erythematosus—Chapter 11

Treatment and Prognosis: Discontinuing the medication or changing to another commonly used medication is considered in a fixed drug reaction (stomatitis medicamentosa). In the case of stomatitis (stomatitis venenata), discontinuing the product responsible is the treatment of choice. Withdrawal of the offending source, such as a particular toothpaste, usually produces results within several days to 2 weeks. Medications such as antihistamines or, in severe cases, epinephrine may be used to manage the symptoms of hypersensitivity over the course of the allergic response. However, avoidance of the trigger agent is important in the management of future episodes. In many cases, no specific agent may be found and the same component may be in other similar products used by the person, making these conditions difficult to control.

NAME: Lupus erythematosus

Etiology: **Lupus** is classified as an autoimmune disease and a type III hypersensitivity reaction (Rubin, 2012). In systemic lupus, although the cause is unknown, there is a breakdown in the normal immune surveillance mechanisms. The body begins to attack its own normal cells. According to the National Institute of Arthritis and Musculoskeletal Diseases (April, 2009), the suspected causative agents are sunlight, stress, hormones, cigarettes, certain medications, and viruses (such as the Epstein-Barr virus) in genetically susceptible individuals.

Method of Transmission: Lupus erythematosus is an autoimmune disease and is not contagious.

Epidemiology: The Lupus Foundation of America estimates that approximately 1,500,000 Americans have some form of lupus (2011). As with most autoimmune-type diseases, females are affected more than males. Lupus is 10 to 15 times more common in adult females, typically affecting women aged 15 to 45 (and predominately those in their 30s), although children and men may be affected as well. The disease is more common in Blacks (1:250) and nonwhite groups such as Latino and Asian (1:1,000). It is estimated that there are 5 million cases of lupus worldwide and approximately 16,000 new cases annually. There is a higher incidence in Europe and Australia than in the United States. In Europe, the highest prevalence was reported in Sweden, Iceland, and Spain (Lupus, 2006).

Pathogenesis: Lupus is a chronic autoimmune disorder that affects the skin surfaces, the organs (mainly the kidneys), joints, serous membranes, and skin, although any organ can be affected. The disorder arises because of an antigen–antibody response that causes inflammation of multiple

organs throughout the body as in a type III hypersensitivity reaction. Antibodies (IgG, IgM, and IgA) are formed against exogenous or endogenous antigens, and complement and leukocytes (neutrophils and macrophages) are often involved. This scenario is typical for most lupus erythematosus.

The oral tissues are also affected and the mucosa can be extremely erythematic and painful. Certain pharmaceutical agents have been implicated in the pathogenesis of lupus, such as hydralazine, lovastatin, penicillamine, recombinant cytokines, L-tryptophan, and procainamide. There is a genetic predisposition to the disease. Lupus is classified into two groups. Discoid lupus erythematosus (chronic form, DLE) accounts for 70% of all cases. Systemic lupus erythematosus (acute form, SLE) which accounts for 10% of cases, is a multisystem disorder affecting the kidneys, joints, heart, lungs, CNS, and the skin. In SLE, the heart may develop thrombus formation and thrombocytopenia may lead to bleeding with anemia due to suppression of the platelet and red blood cell counts. The kidney is also affected, and renal failure is a problem for these patients. Along with the DLE and SLE forms, drug-induced lupus is found in about 10% of cases, and another 10% have a relationship with other connective tissue diseases such as scleroderma. The oral and cutaneous lesions may be seen in varying degrees with all forms of lupus erythematosus. Small, nonbacterial vegetations may form on the heart valves and are called **Libman-Sacks endocarditis**. As with any severe systemic disease, working together with the physician is important and premedication may be needed for certain procedures. The new American Heart Association guidelines should be addressed, but ultimately, each case is certainly unique and the physician should be involved in the decision to premedicate for certain types and procedures. (See Clinical Protocol #17 for antibiotic coverage related to heart conditions.)

Extraoral Characteristics: Weight loss, arthritis, skin lesions, and a classic rash over the nose and malar region (butterfly rash) are common in DLE. Figure 12.28 is an example of the classic rash in the malar region. These features are present in approximately 25 to 40% of patients. Additionally, alopecia and vesiculobullous lesions are commonly found. Figure 12.29 depicts the scalp area of a patient with systemic lupus. Note the ulcers and scabs on the scalp.

FIGURE 12.29. Lupus erythematosus scalp lesion. (Courtesy Dr. Nancy W. Burkhart.)

The disease is associated with endothelial damage to the heart, resulting in an increased incidence of infective endocarditis. Other features of lupus erythematosus include Raynaud phenomenon, photosensitivity, giant cell arteritis, celiac disease, primary biliary cirrhosis, facial and parotid swelling, and potential malignant changes. CNS involvement is sometimes present, and seizures may occur that would warrant clinical consideration. The patient with external lesions may also be sensitive to sunlight both in skin and eye sensitivity.

Perioral and Intraoral Characteristics: Oral lesions are present in all forms of the disease in 25 to 40% of patients, but this is less evident in the milder form. The lesions are characterized by erythematous erosions or ulceration surrounded by a white rim with radiating keratotic striae. The most frequent sites of involvement are the hard and soft palate, buccal mucosa, and the vermilion border of the lips. The gingiva may take on a desquamative appearance, and there is often confusion with other mucosal diseases such as lichen planus, pemphigus, and pemphigoid. Figure 12.30

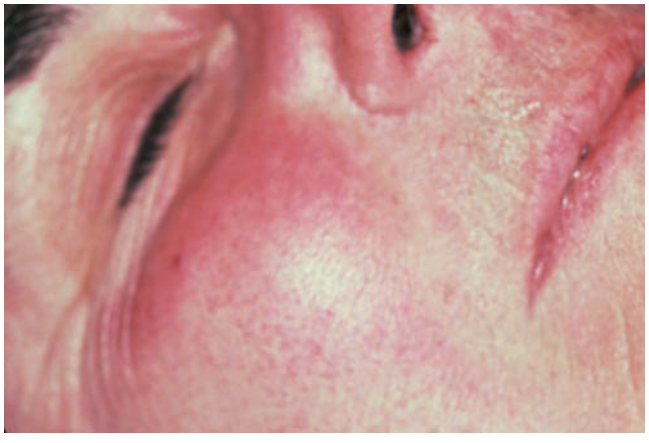

FIGURE 12.28. Lupus malar rash. (Courtesy Dr. Nancy W. Burkhart.)

FIGURE 12.30. Lupus skin lesion. (Courtesy Dr. Nancy W. Burkhart.)

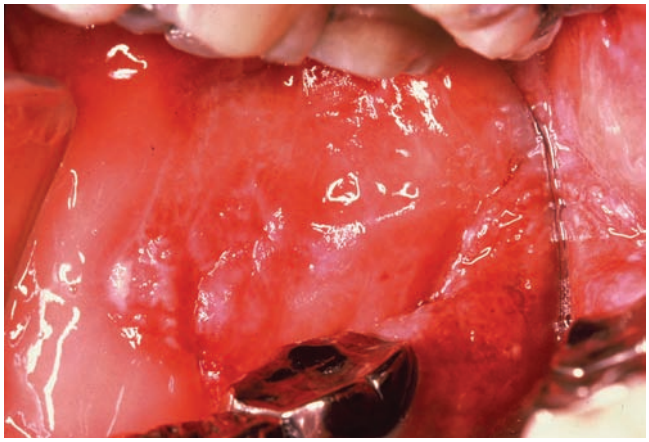

FIGURE 12.31. Discoid lupus oral lesion. (Courtesy Dr. T. D. Rees.)

shows a discoid skin lesion above the eye associated with lupus. Figure 12.31 is an example of the ulcerative mucosa in systemic lupus. A biopsy and immunofluorescence are needed for a definitive diagnosis.

Significant Microscopic Features: Lymphocytic infiltrate, thickened basement membrane zones, and connective tissue are characteristic. The lymphocytic infiltrates are dispersed about appendages and vessels. Oral lesions may be found in all forms of the disease. Other key features of lupus include keratinocyte vacuolization, subepithelial periodic acid–Schiff-positive deposits, lamina propria edema, thickening of the basal cell layer membranes, and a severe perivascular lymphocytic infiltrate. Immunofluorescence is most helpful in differentiating lupus from other skin disorders such as lichen planus, pemphigus, and pemphigoid. Another diagnostic aid is a serologic test for circulating antibodies (antinuclear antibodies [ANAs]). Cell counts, kidney function, and clotting times all contribute to a final report.

Dental Implications: The gingiva may be described as desquamative, and the general description of soreness is a common complaint of patients. In addition, other surfaces may be involved, such as the oropharyngeal mucosa, the larynx, and the epiglottis. Patients may complain of severe dryness of the mouth and other symptoms that are also found in Sjögren syndrome (see Chapter 17 and Clinical Protocol #4). When corticosteroids are used for extended periods, *Candida* infections may occur simultaneously. Treatment of the fungal infection would be needed (see Clinical Protocol #5).

Differential Diagnosis: Lupus must be distinguished from other skin disorders such as the following:

1. Erosive oral lichen planus—Chapter 13
2. Pemphigus vulgaris—Chapter 11
3. Mucous membrane pemphigoid—Chapter 11
4. Erythematous candidiasis—Chapter 14
5. Hypersensitivity reactions—Chapter 12

Some pharmaceutical agents have been implicated in the pathogenesis of drug-induced lupus erythematosus, and patients sometimes experience remission when these products are discontinued. The use of certain medications may present as similar to EM, discussed above. Medications such as lovastatin, penicillamine, L-tryptophan, and procainamide have been implicated.

Treatment and Prognosis: Oral and skin lesions usually respond to topical and intralesional corticosteroids, depending on the severity. Hydroxychloroquine (Plaquenil) is often used, as well as anti-inflammatory agents for milder forms. Antibiotic prophylaxis may be used to prevent bacterial endocarditis if the patient has involvement of the endocardium or heart valves. Additionally, topical corticosteroids and systemic steroids are used to treat the oral lesions for SLE. Intralesional corticosteroids are sometimes used, with variable results. Antimalarial drugs (Plaquenil), gold salts, nonsteroidal anti-inflammatory drugs (NSAIDs), and cyclosporine have been used in the treatment of lupus as well. Depending on the severity of the disease and the degree of systemic involvement, lupus is a chronic, progressive disease, and the treatment of symptoms related to lupus will vary. Renal failure is the most common cause of death. The 20-year survival rate is close to 70%. Careful and nontraumatic maintenance appointments two to three times a year are optimal for maintaining the tissue. Patient education regarding dental products, brushing, and oral dental care aids is very crucial in maintaining good tissue response.

NAME: Crohn disease

Etiology: **Crohn disease** is mentioned here because of the associated oral aphthous ulcers, and it is seen as a chronic condition in patients. The disease was first described in 1932. It is a chronic disease that involves the gastrointestinal tract from the mouth to the anus. Evidence suggests that there is a hereditary component to Crohn disease in 10 to 20% of those affected. Crohn disease is most common in young individuals. Although the etiology is not known, it is thought to be genetically and immunologically mediated.

Pathogenesis: For years, a relationship between vitamin D deficiency has been noted, but it is not known whether the deficiency is a result of inadequate nutrition due to the disease. A recent study by Wang et al. (2010) suggests that vitamin D deficiency may play a role at the molecular level in the development of the disease. It is known that vitamin B and D, folic acid, and other nutrients are poorly absorbed in patients with long-term Crohn disease. Patients may present with oral conditions related to the poor absorption of these nutrients, including pale tissue, papillae atrophy of the tongue, mild fissuring of the tongue, and large aphthous ulcers. Obstruction of bowel with abscess formation is common in long-term Crohn disease with an increased risk of colon cancer.

Extraoral Characteristics: **Pyostomatitis vegetans** is associated with ulcerative colitis as well as Crohn disease. These white, vegetative folds are usually located on the gingiva and indicate that there may be exacerbation of the intestinal

FIGURE 12.32. Crohn disease—pyostomatitis vegetans. (Courtesy of Dr. T.D. Rees.)

colitis. The white folds are painless and contain microabscesses. Figure 12.32 depicts the folds in a young patient. The lips may be involved as well and may appear ulcerative with evidence into the wet line of the lip. The facial and oral characteristics of Crohn disease are within a wide array of idiopathic granulomatous diseases of the oral cavity, lips, and the perioral areas of the face. Figure 12.33 depicts the lip lesions in a young patient, with edema, crusting, and red ulcerative lip appearance.

Perioral and Intraoral Characteristics: The lesions are noncaseating epithelioid-type granulomas. The involved tissue may be fissured, and epithelial hyperplasia is usually present. Intestinal signs and symptoms include abdominal discomfort, anorexia, weight loss, and fever. Oral lesions are reported in up to 20% of the patient population. The lesions may manifest as lobular enlargement of the tongue, soft palate, and labial or buccal mucosa, which may appear to have a "cobble-stoning" effect. The lips may be involved, enlarged gingival lesions may be present, and there is an increased incidence of aphthous ulcers. The lesions are usually slow healing and found in the oral vestibule at the base of the tissue folds. Figure 12.34 depicts an ulceration in the maxillary retromolar area of a patient with Crohn disease.

FIGURE 12.33. Lip lesions of Crohn disease. (Courtesy of Dr. T. D. Rees.)

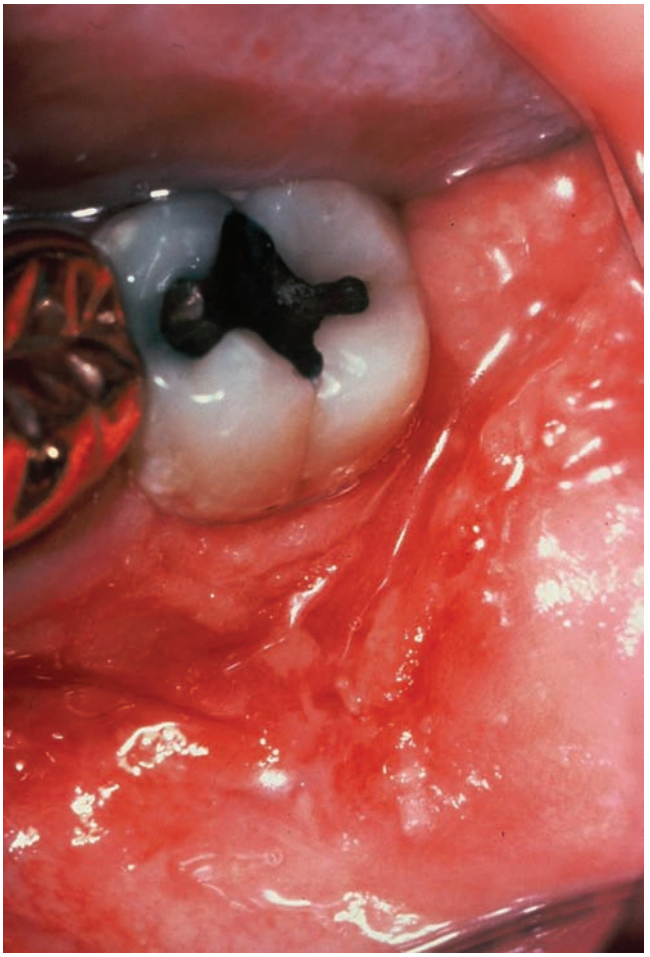

FIGURE 12.34. Crohn disease. (Courtesy of Terry Rees.)

Significant Microscopic Features: The microscopic features include nonspecific focal aggregations of lymphocytes and regular perivascular infiltrates of inflammatory cells. Noncaseating epithelioid granulomas may be found, and multinucleated foreign body giant cells may or may not be present. The overlying epithelium may be normal, hyperplastic, or ulcerated (Fig. 12.35).

Treatment and Prognosis: The diagnosis for Crohn disease is made on clinical signs, symptoms, and biopsy results, and the clinical appraisal alone is not sufficient to diagnose Crohn disease. As presented throughout this chapter, many disease states have an ulcerative clinical appearance. Subtle, less dramatic symptoms with vague, persistent complaints are sometimes ignored for many years before the patient is finally diagnosed.

Management of the intestinal lesions is crucial in the success of treatment. Using systemic corticosteroids, sulfalazine, cyclosporine, or other anti-inflammatory medications is the usual procedure. For oral lesions, the use of topical corticosteroids or intralesional corticosteroids is the treatment of choice. Crohn disease is a chronic disease, and the patient may have remission periods with recurrent episodes.

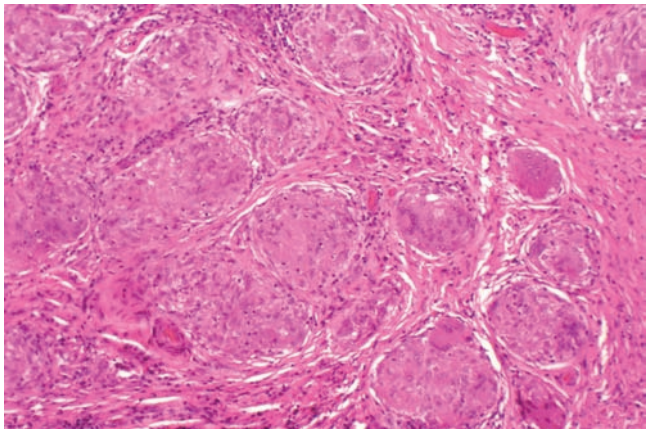

FIGURE 12.35. Histology of Crohn's. (Courtesy of Dr. T. D. Rees.)

Neoplasms

Neoplasia is a general term given to tissue that exhibits abnormal and uncontrolled growth. This section deals with neoplasms in relation to squamous cell carcinoma (SCC), since malignancies seen orally are, for the most part, SCC. Chapter 5 has a comprehensive discussion of the types of cancers, staging, and the behavior and characteristics of various types of cancer. As described in Chapter 5, a neoplasm that does not spread to other tissues (i.e., does not metastasize) is described as benign. A neoplasm that spreads and invades other tissue or organs is termed *malignant* or may be referred to as *cancerous*. In understanding the names assigned to neoplasms, in most cases, the types of tissue that are involved can be determined simply by the name of the neoplasm. For example, tumors that arise from the epithelial tissue are termed *carcinomas*. If the epithelial tissue is of glandular origin, it is called an **adenocarcinoma**. The Latin root *adeno* means gland. A neoplasm of connective tissue, bone, nerve, or muscle is a **sarcoma**.

The most common oral cancer is SCC. The hygienist is sometimes the first person to see an early cancer, so the importance of detection, documentation, and possible referral for a biopsy cannot be overemphasized (see Clinical Protocol 12). When lesions are found and treated early, the patient's likelihood of recovery is increased immensely. The devastation of head and neck surgery can be minimized when early lesions are detected, and the patient's long-term health and long-term quality of life are increased (see Chapter 10).

NAME: Squamous cell carcinoma

Etiology: This section discusses ulcerative changes, since some SCC may have an ulcer-like appearance as they progress. The etiology of SCC is multifaceted. Lifestyle choices, environmental influences, genetic factors, infections (particularly by viruses), and various combinations of these and other items may be responsible in the development of any type of cancer. Although no one cause is accepted in the development of oral cancer, there are factors that have been associated with the development of the disease. Sunlight, tobacco, alcohol, diet, stress, environmental factors such as chemical exposures, and the use of products such as betel quid in certain populations have a strong association. Infections that have been implicated include syphilis, candidosis, and viruses such as the human papilloma virus (specifically HPV-16). Some chemical industrial hazards have been implicated, as evidenced by an increased cancer incidence in workers at woolen textile plants/chemical plants. A higher rate of cancer may be found in association with some mucosal disorders such as oral submucous fibrosis, lichen planus, and other chronic-type ulcerative lesions. In the past few years, inflammation in general has received much attention, and extensive research has focused on the impact of chronic inflammation at the cellular level affecting all areas of the body.

Method of Transmission: Oral cancer is not a contagious disease and has not been documented as such in the medical/dental literature. However, many recent studies have linked the human papilloma virus with certain types of cancers such as cervical cancer. In addition, HPV types 16, 18, 33, and 35 have been implicated in many head and neck cancers (Massano et al., 2006; Ramqvist & Dalianis, 2010). Oral–genital sex has been implicated as a possible mode of transmission related to the HPV-16 cancer association (Gillison et al., 2000; 2008). This is especially important in head and neck squamous cell carcinoma (HNSCC). HNSCC includes cancers of the oral cavity, oropharynx, hypopharynx, larynx, sinonasal tract, and nasopharynx. HNSCC is the sixth most commonly occurring type of cancer.

Epidemiology: The American Cancer Society (2012) estimates about 40,250 (28,540 men and 11,710 women) new cases of oral cavity and oropharyngeal cancer will be diagnosed in 2012. Of these new cases, 7,850 will die of these cancers. SCCs encompass at least 90% of all oral malignancies. Oral and pharyngeal cancers account for approximately 3% of all cancers in the United States. Men exceed women in developing this neoplasm by 1.8 to 1. Although we have seen declines in new cases of oral cancer since the 1970s, The American Cancer Society (2011) reports that approximately one-third of these cancers occur in patients under 55 years old related to the infection with the human papilloma virus. There has been an increase in SCC in women, who have had a much lower oral cancer rate previously, over the past decades. This is probably due to the increase in women who smoke and the use of tobacco products coupled with an increase in alcohol consumption. Approximately 90% of all oral cancers are carcinomas that arise from the surface stratified squamous epithelium. Data from the American Cancer Society (2012) indicate that the 5-year survival rate for localized stages (the cancer has not spread to other sites in the body) is 96%, with a 5-year survival rate of stage IV at 30 to 43%, depending upon the area of the mouth. SCC typically affects an older population group. Half of all oral cancers are diagnosed in persons older than 60 years of age with an average age of 62 years old. However, statistics show an alarming increase in the number of cases involving

those under the age of 40. Some 90% of patients with oral cancers use tobacco, and smokers are six times more likely to develop cancer than nonsmokers. Coupled with alcohol use, the risks are further increased; 75 to 80% of oral cancer patients drink alcohol frequently, placing them at six times the rate of nondrinkers. Interestingly, 25% of people who develop oral cancer have no risk factors. Blacks have a higher risk of oral and pharyngeal cancers, with oral cancer being the fourth most frequent site of cancer in this group. Countries such as Hungary and France have more reported oral cancer cases, with Japan and Mexico reporting much less. HNSCC is the most common form of cancer in India. The incidence of oral cancer in Europe in people aged 20 to 39 years old has increased six-fold. Studies report increased mortality rates for the past two decades in Eastern Europe (La Vecchia et al., 2004). This is also increasingly evident in statistics of SCC of the tongue in adults under the age of 40 in the United States (Schantz & Yu, 2002). Researchers have reported that cancer in younger patients tends to be more aggressive, with a poorer prognosis in these patients. It is speculated (Llewellyn et al., 2004) that because oral cancer is expected to occur in the older population, perhaps there is more of a delay in diagnosis and treatment in younger groups. Additionally, oral cancer is more often being discovered at advanced stages and requires more aggressive treatment. Studies by Watson et al. (2009) found that patients who were recently diagnosed with oral cancer were documented to be at an early stage, if they were under the care of a primary dental professional and had been in for regular dental exam within the past 12 months. According to the American Cancer Society (2012), oral cavity and oropharyngeal cancers occur most often in the following sites: (1) the tongue, (2) the tonsils, and (3) the minor salivary glands. Other risk sites are the lips, gums, floor of the mouth, and other sites. The tongue and the tonsil region have become the high-risk locations because of the association with HPV (Ramqvist & Dalianis, 2010). The lip is a high-risk area as well, and patients should be checked for cancer in this area and encouraged to wear lip balm with sunscreen (see Clinical Protocol #10 and Chapter 23).

Extraoral Characteristics: The external features of SCC and basal cell carcinoma are discussed fully in Chapters 5 and 23. In any oral examination, be sure to check the extraoral sites as well. Have the patient remove eyeglasses so that the area under the frames may be evaluated. This area is a prime location for basal cell carcinoma, and the patient may not view the area themselves in a mirror without their glasses. The area under the frame is often totally missed. Hats and often wigs shield the areas on the head, and skin under these areas should be evaluated as well.

Perioral and Intraoral Characteristics: SCC may show a wide variety of clinical appearances. Many SCC cases exhibit **erythroplakia**, which is a general clinical term for a red patch. Most all lesions having an erythroplakia component are found to be either dysplastic or malignant. Any lesion that has a mixture of red and white color and an ulcerated appearance is highly suspicious. (Erythroplakia and erythroleukoplakia are discussed fully in Chapter 14 and mentioned in Chapter 13.) In addition to being red, erythroplakia often is described as velvety in appearance. The lesions may be homogenous red or have a mixture of red and white components, in which case it is termed **speckled erythroleukoplakia.** Any lesion in the oral cavity has the potential to be malignant or to change in form under certain circumstances. Therefore, every lesion deserves concern. The most frequent sites for oral cancer are found in what may be termed the "drainage" area, comprising the ventral and lateral border of the tongue, the floor of the mouth, the adjacent lingual mucosa, the lingual sulcus, and the retromolar region. The dorsum of the tongue is a low-risk area. The oral pharynx and tonsillar regions (high-risk areas) are often included in general head and neck cancer statistics. Figure 12.36 is an example of SCC of the tonsil; Figure 12.37 depicts SCC of the gingiva. Figure 12.38 shows SCC of the palate, and Figure 12.39 depicts SCC of the tongue, with trauma as well.

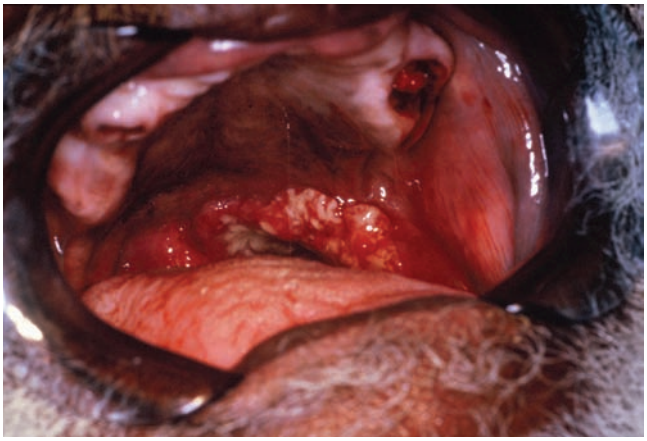

FIGURE 12.36. Tonsillar squamous cell carcinoma. (Courtesy of Dr. Michael Brennan.)

FIGURE 12.37. Squamous cell carcinoma in the gingiva. (Courtesy of Dr. Terry Rees.)

FIGURE 12.38. Squamous cell carcinoma of the palate. (Courtesy of Dr. Michael Brennan.)

The oral pharynx and the tonsillar region is one in which particular attention is warranted and it is overlooked in many cases. Evaluation should include the tonsil and pharyngeal region in a thorough intraoral examination and cancer screening. Although a malignant neoplasm may have many appearances, any abnormal, unexplained lesion should raise a red flag. SCC may initially appear as only a subtle change. Documentation and digital photography can greatly enhance the probability that small changes will be noticed. The lesion may be compared with previous photos and a subsequent referral should be made.

Distinguishing Characteristics: SCC is a great imitator of other disease states. Early cancer can resemble many diseases or can appear essentially very benign initially. It is only after the tissue begins to rapidly grow and change appearance that cancer may be suspected. Unlike other external areas of the body, the patient is usually not aware of these changes, since they are not in visible areas. Unexplained lesions, continued enlargement, and a lesion that does not recede on its own should be evaluated by biopsy. Clinical Protocol 12 discusses various techniques that may be used in early cancer detection when there is a suspected change in tissue.

Significant Microscopic Features: Depending upon the stage of the cancer, cells will present with hyperchromatism, pleomorphism, increased nuclear cytoplasmic ratio, premature keratinization, and formation of spheroidal masses of keratin deep within the epithelium. These nests are called **keratin pearls.** Mitoses are typically increased in number and often abnormal in appearance. Figure 12.40 shows a histology slide that demonstrates the nests of cancerous cells, keratin production, and obvious invasive SCC.

Dental Implications: The dental implications related to SCC are extensive. The principles of detection and diagnosis of SCC are discussed throughout this book, and patients with previous SCCs who are on maintenance therapy must be considered. SCC may recur, and these patients should be carefully monitored for any tissue changes. The practitioner should be alerted to the increased risk of cancer development in patients who have a history of bone marrow transplantation, solid organ transplants, or any other reason for extensive immunosuppression (Sciubba, 2001). The current theory in cancer research is that head and neck cancers develop within a contiguous field of preneoplastic cells. Cells of a field show genetic alterations associated with the process of carcinogenesis even though the tissue appears clinically normal. In other words, even after the carcinoma has been removed, cells at the periphery but within the field may have a tendency to become invasive cancer. These cells

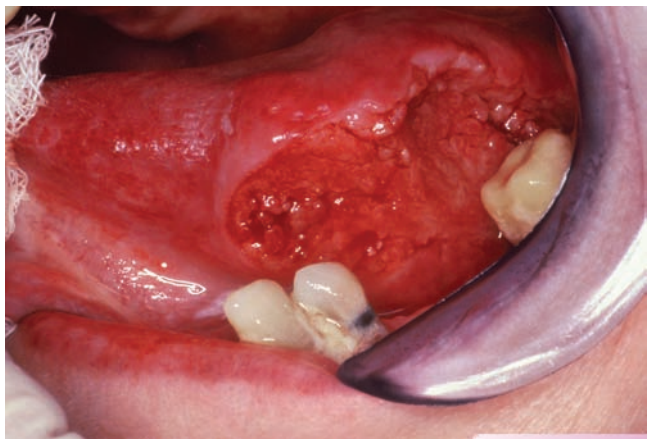

FIGURE 12.39. Squamous cell carcinoma of the tongue. (Courtesy of Dr. Terry Rees.)

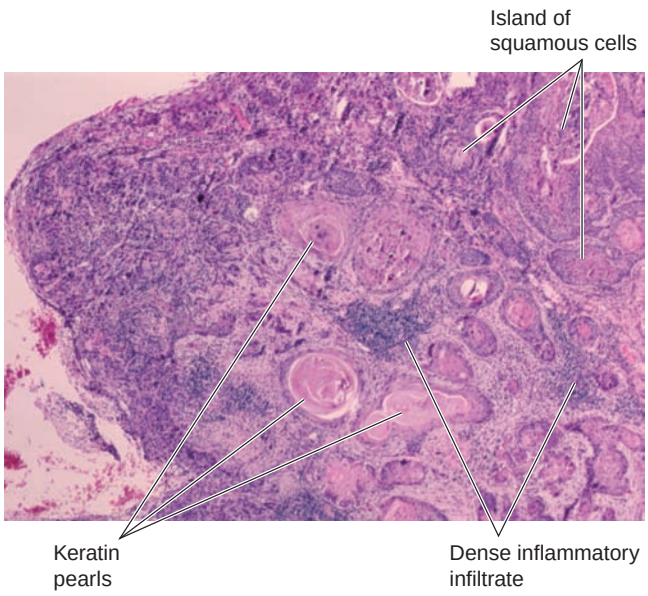

FIGURE 12.40. Squamous cell carcinoma histology. (Courtesy of Dr. Harvey Kessler.)

all share genetic alterations. This differs from a cancer that may recur due to residual cancer cells left after surgery. Development of a secondary primary tumor in the same general area is also a possibility. The theory of **field carcinogenesis**, in practical terms, suggests that medical and dental practitioners should be alerted to any tissue changes in the surrounding areas when a patient has had any type of malignancy (Braakhuis et al., 2005; Tanaka & Ishigamori, 2011).

Differential Diagnosis: Cancer in the early stages is often painless, is white or red or variegated in color, and may present as nodules, indurated masses, patches, or fissured or ulcer-like lesions. Essentially, cancer may have many faces. Early SCC may resemble other benign mucosal lesions. Unrecognized and untreated lesions progress to form the classic indurated fixed ulcer with raised and rolled edges and possible color variation. This emphasizes the importance of the role of the dental hygienist in early detection of cancerous lesions. Adoption of a healthy attitude toward thorough clinical examination and a questioning speculation toward any unaccountable lesion occurring in the oral cavity are critical. If an unexplained lesion does not subside within 2 weeks or if there is obvious concern initially, further examination and possible biopsy are warranted. We suggest that patients be considered for one or several options: (1) biopsied, (2) evaluated further (see Clinical Protocol 12) and referred, or (3) rescheduled for a return visit to evaluate a suspicious area (such as an area that may be frictional).

Treatment and Prognosis: Treatment is primarily based on the stage of the lesions at initial diagnosis. Treatment may consist of surgical excision, radiation therapy, and/or chemotherapy, alone or in combination. The prognosis will depend upon the stage of the cancer but also the location. For example, the prognosis for floor-of-the-mouth cancers is less promising than the prognosis for cancers in the lip area. Additionally, health-related consultation should be part of the dental examination, such as reduction of frictional activities that promote tissue change, diet habits that are detrimental, smoking cessation, alcohol reduction (including alcohol-containing mouth rinses), and adoption of good health habits. This should include counseling on risky-type behaviors as well. HPV-16 continues to be implicated in head and neck cancers (Pannone et al., 2011). The areas in the posterior pharynx and base of the tongue including the tonsil region are very difficult to view and the importance of a thorough head and neck exam cannot be emphasized enough (Siegel et al., 2009; Lingen, 2011).

SUMMARY

- Ulcers may have many causes and may be factitial, traumatic, or iatrogenic.
- Necrotizing sialometaplasia is caused by trauma and salivary gland ischemia in a localized area.
- Syphilis consists of three stages with three types of oral lesions: primary stage, with a chancre-type oral lesion; secondary stage, with mucous patch–type oral lesions; and tertiary stage, with a gumma-type lesion.
- Hutchinson triad involves three factors in the infection of syphilis: inflammation of the cornea, eighth nerve deafness, and dental abnormalities.
- Gonorrhea is caused by *Neisseria gonorrhoeae* (gonococcus).
- Actinomycosis results in external draining fistulas and is caused by *Actinomyces israelii,* a gram-positive bacterium.
- NUG produces a fiery red gingiva with bleeding and has a characteristic fetid odor.
- Organisms found in the natural environment that may enter the body through cuts and the mucous membranes produce deep fungal infections.
- Ulcer-like lesions may have an etiology that is infectious, autoimmune or traumatic, or in some cases malignant, which can be devastating.
- RAUs appear on nonkeratinized tissue.
- RAUs may appear in three types: minor, major, and herpetiform.
- A thorough health history, oral inspection, and the questioning nature of the dental hygienist will ensure that serious disease states are not overlooked.
- Some of the diseases discussed in this chapter are infectious and may continue to progress if not treated.
- Aphthous-like ulcers occur in Behçet syndrome, Reiter syndrome, PFAPA, and Crohn disease.
- Reiter syndrome is a triad of arthritis, urethritis, and conjunctivitis.
- Many lesions have subtle appearances in the early stages, and it is important to evaluate any oral lesion thoroughly and to fully scrutinize those that lack an established cause.
- EM has characteristic “target lesions” or “iris lesions” on the skin.
- Hypersensitivity reactions may be related to medications and products that the patient is using, either systemically or topically.
- The dental hygienist is in a unique position to detect early premalignant and malignant lesions that are in the head and neck area.
- SCC may have varied appearances and must be detected early.
- Patients who have oral cancers detected in an early stage will have less surgery, less adjunctive therapy, and a higher rate of recovery long-term.
- Patients who wear eyeglasses often view the facial area with their glasses on, and sometimes, the rims of the glasses mask lesions lying under the frames.
- Having patients remove eyewear, hats, and anything obstructing the head and neck area allows the clinician a clear view of crucial areas.

CHAPTER REVIEW

Case Study 12.1

A 23-year-old male comes to your office for an appointment. His health is good, and he has no major complaints or problems. He has an appointment as a new patient, and his only oral complaint is about some swelling on the LL mandible region. He has noticed that he has some skin problems also on the same side. He complains about some exudates from the facial outbreaks. As you scan the patient's face, you notice that the LL facial area does appear swollen, and the same area appears to have some surface lesions.

1. What questions would you ask the patient?
2. What possibilities of disease states would you consider for the facial lesions?
3. Why would you not consider a dermatology condition such as acne?
4. What features would you search for related to the skin lesions?

You learn that the patient had a third molar extraction a few months prior to the present appointment and has had no problems. Intraorally, the extraction site appears to be healing. There is some swelling in the second and third molar region, but he does not report any pain (Fig. 12.41A).

5. What connections should be considered between his intraoral condition and the extraoral condition?
6. What systemic problems or disease states would you consider that might be relevant in this case?

After further examination, you notice a small opening on the lower external jaw area (Fig. 12.41B).

7. What would you consider at this point?

FIGURE 12.41. A, B. Mandible and third molar area. (Images courtesy of Dr. John Jacoway.)

For answers and additional review activities, log in to **thePoint.lww.com**

Case Study 12.2

Miguel, a 26-year-old male, presents at your office for a routine semi-annual dental hygiene appointment. Miguel's medical history is unremarkable and he appears to be in good health. He takes no medications, but as you review his medical history with him, he mentions a current and recurring problem with red and irritated eyes for which he says he has an appointment with an eye doctor next week. He also had a urinary tract infection a week ago. His dental history has not changed in 6 months. You perform the head, neck and intraoral exam, noting both the red irritated eyes and the lesion pictured in Figure 12.42. He describes the 2-cm ulceration on his tongue as very painful and he has continued to traumatize the lateral border of the tongue because of previous ulcer-like lesions and scarring of the tissues.

1. Describe the lesion using appropriate dental terminology.
2. What type of ulcer does this appear to be?
3. What follow-up questions would you ask this patient to learn more about the tongue lesion?

4. Remembering his statement about recurrent eye irritation, what questions might you want to ask Miguel about his general health?
5. Which disorders (from this chapter) would you include in a differential diagnosis for this lesion? List them from most likely to least likely.

For answers and additional review activities, log in to **thePoint.lww.com**

FIGURE 12.42. Tongue ulcerated lesion. (Images courtesy of Dr. J. Ship.)

Critical Thinking Activity

Figure 12.43 depicts a heavy cocaine user. How is it possible that this person will be diagnosed as having erythema multiforme (EM) as well as having a factitial injury? Could one cause the other?

FIGURE 12.43. Cocaine user. (Courtesy of Dr. T.D. Rees.)

Portfolio Possibilities

- Develop an information sheet for patients who suffer with chronic aphthous ulcers. Please use Clinical Protocol #8 for RAUs and individualize your information for various patients. Include "trigger" mechanisms and environmental factors associated with the condition. Clinical photos may be part of your educational information.
- Develop a procedure list for new and recall patients that outlines a thorough oral exam and medical history update and helps in screening visible external surfaces for skin cancer. Involve your entire office staff in this procedure.
- Develop a diet diary for the patient with aphthous ulcers using the Clinical Protocol #8 information. Personalize the diet diary to your own clinic or office with name, contact information, etc.
- Determine the clinical protocol for your office on oral cancer. A set of guidelines that state your referral protocol and procedures that will be developed and followed when evaluating any new lesion is an important statement for your office.
- Develop a patient education sheet for patients who are undergoing or have been through cancer surgery and radiation treatment and are having problems related to these factors. The clinical protocol on xerostomia would be most helpful to include, as well as the protocol on radiation mucositis. You should include something on diet-related suggestions as well.

Media Menu

Web Sites

Centers for Disease Control and Prevention: Emerging Infectious Diseases journal
http://www.cdc.go/ncidod/eid/index.htm

Centers for Disease Control and Prevention: Division of Sexually Transmitted Diseases Prevention
http://www.cdc.gov/std/

Lupus Foundation of America, Inc.
www.lupus.org

World Health Organization
http://www.who.int/en/

Study Tools

Take advantage of additional online resources to help you study and ace your exams!

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- Additional case studies and answers
- Interactive quiz bank with answer feedback
- Fully searchable e-book for quick lookup and studying on-the-go
- Expanded Media Menu with direct links to related Web sites and multimedia resources
- Supplemental references

thePoint Online resources and links are available at http://thepoint.lww.com/DeLong2e

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NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Traumatic Ulcer	Trauma to the tissue anywhere in the mouth	External forces including brushing and cheek chewing	May be bleeding, loss of epithelial covering, crusting, crater-like lesions	Nonspecific. Inflammatory process, loss of epithelium with fibrinous exudate.	Ulcers heal in about 7 d. Mild-to-moderate discomfort may require light medication in major cases.	None unless a bacterial infection occurs. Scar tissue may make future ulcers more prevalent.
Necrotizing Sialometaplasia	Trauma to the area of the palate	Benign entity occurring at the juncture of soft and hard palate	Elevated mass that becomes ulcerative	Necrosis of the salivary gland duct. There is squamous metaplasia of the salivary duct epithelium.	Analgesics but no surgical interventions	A biopsy should be taken to rule out more serious conditions such as mucoepidermoid carcinoma.
Syphilis	Sexually transmitted	Spirochete *Treponema pallidum*	Chancre, mucous patch, and gumma	The organism appears "corkscrew-like"	Standard treatment is penicillin.	Hutchinson triad: inflammation of the cornea, eight nerve deafness, and dental abnormalities, i.e., mulberry molars and Hutchinson incisors
Gonorrhea	Sexually transmitted	Bacteria *Neisseria gonorrhoeae*	Oral pharynx, tongue commonly affected with ulcerative lesions	Macrophages and lymphocytes predominate.	Antibiotic therapy and patient education	Oral lesions are present and a correct recognition/diagnosis is crucial.
Actinomycosis	Associated with tissue trauma	Bacteria *Actinomyces sraelii*	Ulcerative with exudate associated with ulcer. A fistula may lead to external facial areas.	Identified through cultures. Sulfa granules are present and are seen as yellow grainy particles.	High-dose penicillin is required and may be needed for extended periods of time.	Other serious disease states may be present such as AIDS and the body resistance is in a lowered state.
Necrotizing Ulcerative Gingivitis (NUG)	Infectious disease of gingivae. Lowered state of health and poor nutrition are key factors.	Numbers of spirochetes *Prevotella intermedia*, hemolytic streptococci, Actinomyces, Treponema, and Fusobacterium species are common.	Fetid odor, Gray pseudomembrane forms over necrotic gingiva. Spontaneous bleeding.	Mixed flora of spirochetes	Oral hygiene is maintained after debridement. Oral rinses, proper diet, stress reduction, home care instructions including brushing and flossing. No ultrasonic devices are used to keep aerosol production to a minimum. Peroxide and water or chlorhexidine 0.12%	The papillae do not return to normal and suffer the damage of the infection with blunting.
Deep Fungal Infections	Arise from the soil, bird/ bat droppings, decaying vegetation	Infections occur in the internal organs and submucosal connective tissue.	Lesions are ulcerative, necrotic, and pseudomembranous.	Observed through special cultures and viewed microscopically	Treatment depends on the specific agent. Antimicrobial agents are administered. Recovery depends upon the patient's ability to fight infection.	Identifying the agent is important so that treatment is specific. Referring the patient to the correct specialist is crucial, for instance, to a pulmonologist for lung issues.
Aphthous Ulcers: Minor, Major, and RAU Herpetiform	Not completely understood but associated with triggers such as trauma	Associated with diseases such as Crohn's, Reiter's, Behçet's, PFS, lupus, celiac sprue, and ulcerative colitis.	Occur on nonkeratinized tissue and exhibit a yellow-to-white pseudomembrane with an erythematous border—halo appearance	Exhibit lymphocytes, macrophages, and mast cells	Palliative, with warm saline and bicarbonate rinses. Orabase Soothe "n" Seal to cover tissue. Viscous lidocaine mixed with diphenhydramine elixir is sometimes recommended. See Clinical Protocol #8.	Pain may be an issue for many patients and treatment may be postponed. Trauma from dental procedures may cause outbreaks as well. Other disease states may be present that have aphthous ulcers as a characteristic. Frequent outbreaks may be considered as an indicator of other disease states.
Behçet Syndrome	Inflammatory disorder of unknown cause	Rare multisystem disorder	RAU minor, genital ulcers, and ocular lesions	Polymorphonuclear leukocyte chemotaxis and chemotaxis hyperfunction	Topical steroid with cyclosporine. Lesions can be controlled.	Cyclosporine may produce gingival hyperplasia. Chronic disease states need to be closely watched.

Chapter 12 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Reiter Syndrome	Abnormal immune response	Exposure to venereal disease or gastrointestinal disease; HIV exposure	Aphthous ulcers, ocular inflammation, small joints affected. Achilles tendon, weight-bearing joints affected.	Microscopically resembles psoriasis	Nonsteroidal anti-inflammatory medications. Disease lasts from weeks to months.	Dental treatment should be postponed until lesions are healed. Long-term, condition may lead to arthritis.
Erythema Multiforme (EM)	Exposure to herpes, tuberculosis, histoplasmosis	Genital, ocular, and oral lesions occur.	Stevens-Johnson syndrome is a severe form of erythema multiforme. Target or iris lesions are classic.	Epithelial hyperplasia, spongiosis, vesicles, lymphocytic infiltrate	Short-term corticosteroids	Recurrent lesions are possible in 25% of the cases.
Hypersensitivity Reactions	In the mouth, most are delayed hypersensitivity reactions.	Contact with product or medication causing reactions	Angioedema, urticaria, vesicles, and rash with macules may be present.	Nonspecific features. Spongiosis, lymphocytes, perivascular infiltration.	Withdrawal of the offending product	Sometimes dental products may contribute to sensitivity, for example, latex and flavoring agents/tartar control products in toothpaste. Substitute alternative materials/products as needed.
Lupus Erythematosus	Autoimmune disease and a type III hypersensitivity reaction	Affects organs especially kidneys. Arises because of antigen–antibody response. Causes inflammation of most organs. Antibodies IgG, IgM, and IgA are formed against antigens.	Erythema and painful ulcers. Discoid lupus is most common in 70% of cases and affects skin. Butterfly rash or malar rash is characteristic. SLE is the systemic form in 10% of cases and is multisystem. 10% are in conjunction with other autoimmune diseases. 10% are drug induced.	Lymphocytic infiltrate, thickened basement membranes, and connective tissues. Keratinocyte vacuolization, perivascular lymphocyte infiltrates.	Mucosal lesions respond to corticosteroids, intralesional corticosteroids. Also, antimalarial drugs, gold salts, nonsteroidal anti-inflammatory drugs, and cyclosporine.	Gingiva is described as desquamative, sore, and dryness is reported. Oropharyngeal tissue may be involved. Candida is a common problem with dryness and with corticosteroid use.
Crohn Disease	Most common in young individuals and there is a hereditary component.	Chronic disease affecting the intestinal tract from the mouth to the anus. Discomfort in the abdomen, anorexia, and fever.	Lips may be ulcerative; lobular enlargement of the tongue, soft palate, and labial/buccal mucosa. Increase of aphthous ulcers. Absorption of nutrients may make the tissue pale and cause loss of papillae on the tongue.	Focal aggregations of lymphocytes and regular perivascular infiltrates of inflammatory cells. Noncaseating epithelioid granulomas. Giant cells and overlying epithelium may be ulcerated or normal.	Corticosteroids, sulfasalazine cyclosporine, anti-inflammatory medications. Intralesional corticosteroids may be used for oral ulcerations. Long-term Crohn disease may develop into colon cancer and part of bowel may need removal.	Crohn disease is a chronic-type disease with periods of remission. Careful use of dental products is essential; harsh debridement may cause increased pain for the patient. Gentle procedures are best. *Pyostomatitis vegetans* may indicate exacerbation of intestinal lesions. They are vegetative folds containing microabscesses.
Squamous Cell Carcinoma (SCC)	Oral cancer is increasing in the <40-year-old group. HPV may be implicated in certain cancers.	Base of the tongue and tonsillar region cases are being reported at increased rates. High-risk areas include the lateral border of the tongue and the floor of the mouth. Tobacco and alcohol are known risk factors for oral cancer.	Red, white, or mixed lesions are always suspect and should be fully evaluated. Chronic disease states may mask appearance of frank squamous cell carcinoma.	Nest of keratin formations (keratin pearls). Islands of squamous cells, dense inflammatory infiltrate. Preneoplastic cells may be evident or not visible in microscopic review. Pleomorphism, hyperchromatism, increased nuclear cytoplasmic ratio.	Treatment is based on the stage of the lesion. Surgical excision, radiation, and chemotherapy are common approaches. Lasers may be used in some premalignant lesions.	Frequent recall exams with oral cancer screening including palpation are crucial because of possible recurrence of SCC. Making the patient aware of his or her own ability to do self-exams is important. This does not take the place of a dental professional conducting an oral cancer–screening exam but is rather an adjunct. Dental documentation is important with regular digital images made to capture the clinical appearance of the areas of concern for later comparison.

CHAPTER 13

Lesions in Shades of Red and Purple

KEY TERMS

Candidosis (candidiasis)
Civatte bodies
CREST syndrome
Diascopy
Dysphagia
Ecchymoses
Erythroplakia (erythroplasia)
Fibrinous
Giant cell epulis
Hamartoma
Hemangioma
Hematoma
Hereditary hemorrhagic telangiectasia
Hypersensitivity
Involution
Kaposi sarcoma
Lichen planus
Lichenoid reaction
Lingual varix
Lymphangioma
Neoplasm
Peripheral giant cell granuloma
Perlèche
Petechiae
Phlebolith
Plasma cell gingivitis
Purpura
Pyogenic granuloma
Rendu-Osler-Weber disease
Scleroderma
Speckled leukoplakia (erythroplasia)
Spongiosis
Thrill
Thrombosis
Varices
Varicosity
Vascular formations
Venous varix
Violaceous

LEARNING OUTCOMES

1. Define the key terms used in this chapter.
2. List a variety of lesions that appear red to purple in color.
3. Describe the clinical features of each of the lesions discussed in the chapter.
4. Discuss the similarity and differences in the ecchymoses, petechiae, and purpura.
5. Describe the difference between a hypersensitivity reaction and an anaphylactic reaction.
6. Describe the clinical similarities and differences of the pyogenic granuloma and the peripheral giant cell granuloma (PGCG).
7. Describe the etiology and clinical characteristics of the petechiae, ecchymoses, and purpura.
8. List and describe the two major acute forms of candidiasis that appear red in color.
9. Discuss, describe, and differentiate between a varicosity, a hematoma, and a lymphangioma. Explain how you would determine the difference.
10. Describe the etiology and common locations of acquired vascular lesions.
11. List the six forms of oral lichen planus and describe each type.
12. Describe the difference between oral lichen planus and an oral lichenoid reaction.
13. List the treatment options for oral lichen planus.
14. Discuss the importance of lesions called erythroplakia. Describe the characteristics of these types of lesions and why diagnosis with biopsy and/or monitoring is so important.
15. List the significance of hereditary hemorrhagic telangiectasia with regard to the patient's general health and oral health.

CHAPTER OUTLINE

Traumatic or Inflammatory Lesions
- Pyogenic granuloma
- Peripheral giant cell granuloma (giant cell epulis)
- Petechiae, ecchymoses, and purpura

Immune System Disorders
- Lichen planus
- Hypersensitivity reactions

Infections
- Candidosis (candidiasis)

Neoplasms
- Kaposi sarcoma
- Erythroplakia (erythroplasia)

Vascular Malformations
- Varicosity (varix)
- Congenital hemangioma (strawberry nevus)
- Lymphangioma
- Hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber disease)

RELATED CLINICAL PROTOCOLS

#2 Applying Topical Corticosteroids in the Mouth
#3 Maintenance Appointment Guidelines for the Patient with a Mucosal Disease
#4 Treating Patients with Xerostomia
#5 Diagnosing and Treating Patients with *Candida*
#6 Treating Patients with Sensitivity to Flavoring Agents
#10 Patient Education: UVA/UVB Skin Protection
#12 Adjunctive Oral Premalignant Screening Devices
#25 How to Utilize Nutrition Counseling in Practice
#27 Motivational Interviewing for Behavior Change

Traumatic or Inflammatory Lesions

The oral cavity is an area of the body in which the tissues are subjected to constant forces, trauma, and tissue laceration. Most of the time, the trauma is mild. For example, occasional cheek bites, palatal injury caused by a sharp food product, or trauma from a new toothbrush are examples and common occurrences. Most often, these injuries are small and heal within a day or so. However, chronic trauma and tissue irritation over an extended period produce a different type of tissue response. This includes an exuberance of tissue formed in response to the injury and often some damage caused to the surrounding tissue. This section discusses the types of injuries to the tissue that cause the tissue to produce even more connective tissue, initiate an inflammatory response, and promote increased growth of the tissue.

NAME: Pyogenic granuloma

Etiology: **Pyogenic granulomas** are benign solitary vascular growths that are inflammatory lesions producing exuberant tissue responses to trauma or local irritation. Other well-known names for these lesions include *pregnancy granuloma, pregnancy tumor,* or *epulis gravidarum*. The lesions often appear in pregnancy because of physiologic changes that take place during pregnancy due to the increase in hormones. The pyogenic granuloma is associated with trauma and reaction to a foreign substance such as calculus, in addition to hormonal changes. Multiple etiologies have been cited, such as drugs, hormones, foreign irritants, and systemic involvement such as leukemia. Occurrences have been reported in extraoral granulomas (Goncales et al., 2010) such as the lip region, and some rare cases of multiple intraoral pyogenic granulomas have also been reported. (Shivaswamy et al., 2011)

Method of Transmission: Pyogenic granuloma is neither a contagious entity nor an infectious lesion. An irritant producing an inflammatory response usually initiates this response.

Epidemiology: Puberty and pregnancy may make a person's tissue more susceptible to the development of a pyogenic granuloma. The oral pyogenic granuloma is seen more often in females than in males because of hormonal factors and usually occurs in the second decade of life. Over 75% of oral granulomas appear on the gingiva. The pyogenic granuloma has been found in the palate, tongue, oral mucosa, and the lips. Because of the hormonal connection, many are found in women in childbearing years.

Pathogenesis: A pyogenic granuloma results from chronic trauma or an irritation process. There are no specific pyogenic (pus-producing) organisms associated with the lesion, even though the term *pyogenic* would indicate a pus-producing lesion. The term pyogenic is misleading.

Extraoral Characteristics: Pyogenic granulomas may occur on other mucosal surfaces such as the eye, colon, or external body surfaces.

Perioral and Intraoral Characteristics: The lesion appears bright red in most instances, but the color can vary into shades of pink, depending upon the age of the lesion, with younger lesions appearing more red. At times, the inflammatory tissue will be ulcerated and then be replaced with a more fibrinous tissue, making it appear yellow. Initially, young pyogenic granulomas appear brighter red, with older lesions becoming various shades of pink with a somewhat more fibrotic appearance. The lesion can take various forms and appear more pedunculated (stalk-like) or more sessile (flat-based) depending upon the location and cause. The surface of the lesion may be lobular, smooth, or even appear more papillary. Generally, the lesion occurs on the maxillary anterior gingiva, lower lip, tongue, and buccal mucosa. Lesions range in size from a few millimeters to several centimeters. Pyogenic granulomas are painless and without exudate. Figure 13.1 shows a pyogenic granuloma

FIGURE 13.1. Pyogenic granuloma. (Courtesy of Dr. E.J. Burkes.)

on the maxillary anterior arch. Figure 13.2 depicts a pyogenic granuloma on the lateral border of the tongue. Figure 13.3 shows the histology of a pyogenic granuloma. Note the multiple capillary channels within the specimen.

Distinguishing Characteristics: The combination of hyperplastic granulation tissue and the large number of capillaries causes the pyogenic granuloma to have its characteristic red color. The lesions occur in soft tissue areas such as the gingiva.

Significant Microscopic Features: The pyogenic granuloma is not a true granulomatous inflammatory lesion, but rather an exuberant mass of hyperplastic granulation tissue. This condition involves a chronic inflammatory process, and, occasionally, there is some evidence of tissue repair. As the tissue repair occurs, the lesion becomes more **fibrinous** and may take on the appearance of a fibrinous connective tissue with a slightly yellow hue.

Dental Implications: Pyogenic granulomas should be excised completely so that the lesion does not reoccur since recurrence is a factor with these lesions. Pyogenic granulomas that occur during pregnancy related to hormonal changes may shrink or completely diminish after the pregnancy.

FIGURE 13.2. Pyogenic granuloma. (Courtesy of Dr. Terry Rees.)

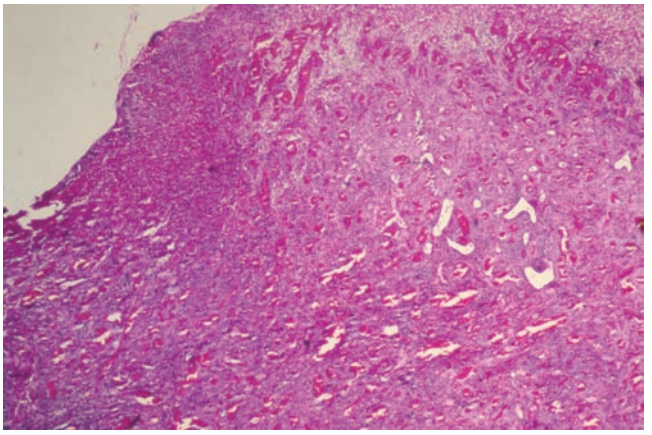

FIGURE 13.3. Pyogenic granuloma histology. (Courtesy of Dr. Denis Lynch.)

Differential Diagnosis: Other lesions that may be a part of a differential diagnosis are the following:

1. Peripheral giant cell granuloma—Chapter 13
2. Fibroma—Chapter 17
3. Kaposi sarcoma—Chapter 22. Because of the highly vascular appearance of the pyogenic granuloma, **Kaposi sarcoma** (red/blue color) may have a similar tissue appearance in some cases and should be ruled out.
4. Neoplasm— Chapter 17 and 22. Any lesion should be considered a neoplasm until an etiology and diagnosis are determined.

Treatment and Prognosis: When the pyogenic granuloma occurs during pregnancy, the growth often subsides after delivery when hormones are at a consistent and reduced level. If the growth does not subside, it is surgically removed but may recur if all affected tissue has not been removed. Large defects may occur, depending upon the size of the growth and the extent of tissue removal, and corrective surgery may be needed to restore the surrounding tissue to a normal appearance. Good results are reported using the carbon dioxide laser (Rossman, 2011). Chemical aids such as chlorhexidine gluconate mouth rinses are recommended; thorough scaling procedures and excellent home care instructions for plaque reduction are needed. Warm, saltwater rinses are helpful in healing the tissues. In other cases, lasers and cryotherapy may be used to remove the lesion. The prognosis is excellent.

NAME: Peripheral giant cell granuloma (giant cell epulis)

Etiology: **Peripheral giant cell granulomas (PGCGs)** are reactive hyperplastic responses to tissue injury, producing an exuberance of tissue in the area of injury.

Method of Transmission: The lesion is localized and not contagious.

Epidemiology: The lesions may occur at any age, but most are reported to occur in the fifth to sixth decades of life. The lesion is less prominent in males, with about 60% occurring

in females. The PGCG is the least frequently seen of the reactive-type lesions of the gingiva.

Pathogenesis: PGCG is a response to injury or trauma causing the connective tissue to respond with a more hyperplastic tissue. The lesions arise from the periodontal ligament or periosteum as a result of chronic irritation or chronic trauma. Sometimes, there is alveolar bone involvement with destruction if not treated. Precipitating factors include tooth extraction, plaque and calculus, faulty dental restorations, or dentures.

Extraoral Characteristics: The PGCG is found on oral tissue and does not exhibit any extraoral characteristics unless the lesion becomes very large, with protruding tissue becoming visible in the anterior region.

Perioral and Intraoral Characteristics: The lesion is found on the gingiva or edentulous ridge, and it is usually forward of the molar region. The lesions can be in the range of 1 to 2 cm. They are normally deep red or bluish purple and are reported to be more bluish than the pyogenic granuloma, which is often a deep red. They can be soft to somewhat firm and smooth in texture. Depending upon the degree of ulceration, they may bleed and are clinically very similar to the pyogenic granuloma but can be distinguished by the characteristic giant cells seen during microscopic examination. Figure 13.4 depicts a PGCG between teeth 10 and 11.

Distinguishing Characteristics: The multinucleated giant cells that make up the tissue when seen microscopically distinguish the lesion. PGCG is microscopically similar to the central giant cell granuloma discussed in Chapter 18. The PGCG is found on the gingiva whereas the pyogenic granuloma can be found in any soft tissue location.

Significant Microscopic Features: The PGCG is composed of fibroblasts and multinucleated giant cells with inflammatory cells within the lesion. The pyogenic granuloma and the PGCG are distinguishable microscopically. The pyogenic granuloma is vascular, while the PGCG exhibits numerous multinucleated giant cells with abundant small capillaries. Figure 13.5 depicts the histology of a PGCG. Note the abundant giant cells within the specimen.

FIGURE 13.4. Peripheral giant cell granuloma (PGCG). (Courtesy of Dr. Michael Brennan.)

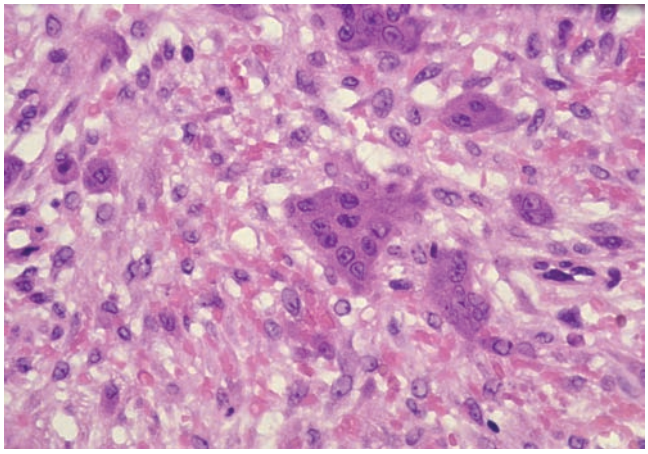

FIGURE 13.5. Histology of a PGCG. (Courtesy of Dr. Denis Lynch.)

Dental Implications: The PGCG can cause bone resorption. This is in contrast to the pyogenic granuloma. Depending upon the location, the PGCG may be observed radiographically when on the edentulous ridge.

Differential Diagnosis: Clinically, the appearance is very similar to that of the pyogenic granuloma. Considerations would be the following:

1. Pyogenic granuloma—Chapter 13
2. Neoplasm—Chapter 17
3. Central giant cell granuloma—Chapter 18

Treatment and Prognosis: When the entire lesion has been completely removed, the prognosis is excellent. The periosteum and the periodontal ligament must be removed with the lesion to avoid recurrence. In addition, the local irritant must also be identified and removed.

NAME: Petechiae, ecchymoses, and purpura

Etiology: **Petechiae, ecchymoses,** and **purpura** are hemorrhages in the soft tissue due to either trauma or blood dyscrasias. When caused by blood dyscrasia, the lesions are usually the result of fewer than normal platelets in the patient's blood and/or clotting factor problems.

Method of Transmission: The lesions that are identified as petechiae, ecchymoses, or purpura are not contagious and not transmitted to other individuals.

Epidemiology: Those of any age may be affected, and there is an equal predilection for males and females.

Pathogenesis: Both petechiae and ecchymoses arise from several sources. Traumatic injury is the major source, such as biting the oral tissues, trauma due to an object such as a finger (often used by patients who engage in disordered eating practices) (see Clinical Protocol #9), fellatio, and factitial injuries (see Chapter 12). Commonly this involves the cheek, tongue, palate, oropharyngeal areas, and lips. Additionally,

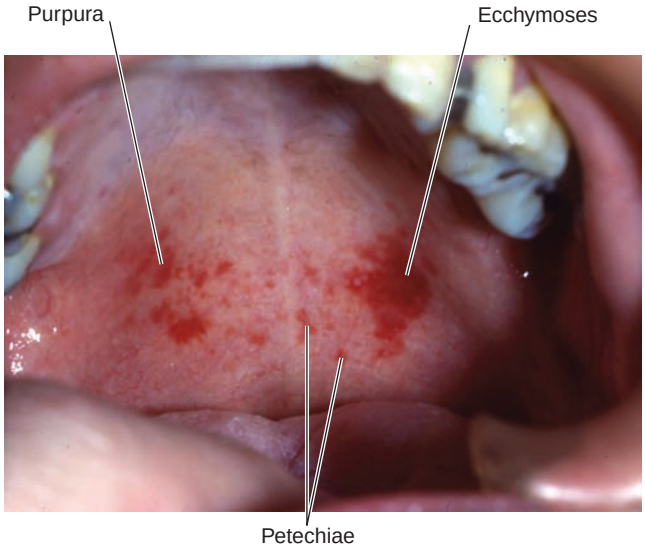

FIGURE 13.6. Petechiae, ecchymoses, and purpura. (Courtesy of Dr. Harvey Kessler.)

the injury may be iatrogenic (see Chapter 12), such as a dental procedure that causes ecchymoses from a handpiece or saliva ejector or just operator error such as anesthesia or impression tray misplacement. Dentures or poorly fitting appliances are another source of this type of injury. The second source of injury to consider is systemic disease such as blood dyscrasias. One such example would be the petechiae and ecchymoses associated with certain blood disorders such as monocytic leukemia and other forms of leukemia. Other blood dyscrasias also have oral manifestations producing petechiae, ecchymoses, and purpura (see Chapter 9). The dental hygienist can be instrumental in referring the patient to a physician for treatment when a traumatic injury factor has been ruled out. Frequent nosebleeds, bruising, and evidence of frequent petechiae, ecchymoses, or purpura all warrant consideration of systemic disease. Figure 13.6 depicts petechiae at the midline of the soft palate, ecchymoses (area on the left side of the palate, left of the midline), and purpura (large area on the right side of the palate, right of the midline). Figure 13.7 shows petechiae on the palate due to trauma related to food.

FIGURE 13.7. Petechiae. (Courtesy of Dr. Michael Brennan.)

Extraoral Characteristics: When pressure is applied, these lesions do not blanch since the hemorrhage is blood that has pooled in the area. If blanching occurs, the practitioner should consider if the lesion might be vascular. The clinician should not be able to stop the flow of blood to the area by applying light pressure, as would be possible with a venous-type lesion.

Perioral and Intraoral Characteristics: Bleeding that results from platelet deficiency occurs in small blood vessels and is characterized clinically by **petechiae.** Petechiae are defined as any tiny, perfectly round, purplish-red spots that appear on the skin as a result of minute intradermal or submucosal hemorrhage. They are small, ranging from 1 to 2 mm, and may be associated with certain disease states such as blood dyscrasia or trauma. **Purpura** refers to focal, circumscribed hemorrhagic lesions in the mucous membrane surfaces that are larger than a petechia and less than 1 cm. Purpura may be associated with platelet abnormalities, bleeding disorders, trauma, or Rocky Mountain spotted fever. Purpura is a symptom rather than a disease entity. Depending upon the cause of the purpura, petechiae, or ecchymoses, the patient may also have associated nosebleeds, frequent bruises, and gingival bleeding. **Ecchymoses** may be described as hemorrhagic spots in the skin or mucous membrane caused by the extravasation of blood into the subcutaneous tissues. The skin areas are larger than purpura and measure over 1 cm (see Box 13.2). These lesions differ from the varicosities discussed later in this chapter, which involve a vein or vascular component. Ecchymoses, petechiae, and purpura do not involve the blood vessels but are formed by a collection of blood located directly under the skin surface. Ecchymoses may be associated with bleeding disorders and hemophilia-related disorders. In hemorrhagic disease, the lesions can appear as blood blisters in the oral cavity.

Distinguishing Characteristics: Petechiae, ecchymoses, and purpura do not blanch and may be distinguished from the venous-type lesions easily using **diascopy** (using a glass slide with applied pressure). Petechiae, ecchymoses, and purpura are pooled blood directly under the skin surface as opposed to varicosities discussed later in this chapter that involve venous blood flow, which may be stopped and observed under the slide.

Significant Microscopic Features: Not applicable

Dental Implications: Identification of blood disease and dyscrasias is important in seeking medical treatment for the patient. Additionally, those patients under care for blood diseases may need special precautions when dental treatment is necessary.

Differential Diagnosis: Some considerations may be the following:

1. Blood platelet abnormalities—Chapter 9
2. Hemorrhagic diseases—Chapter 9
3. Trauma—Chapter 12

4. Bone marrow disorders such as myeloma—Chapter 5
5. Disordered eating practices—Clinical Protocol #9
6. Trauma induced by fellatio

Treatment and Prognosis: Treating the underlying cause or removing sources of trauma is needed to stop the development of petechiae, ecchymoses, and purpura. The prognosis depends upon the cause of the lesion, such as a traumatic lesion as opposed to one that is associated with disease states. These types of lesions associated with trauma usually subside within a week or more when the offending source is removed.

Immune System Disorders

The immune system (discussed in Chapter 4) is the body's major source of defense against disease. The immune system must recognize and differentiate pathogens from the normal cells in our bodies. The conditions listed in this section are affected by the immune system, have oral manifestations, and appear in shades of red, blue, or purple.

NAME: Lichen planus

Etiology: Wilson (1869) originally documented cases of patients with oral lichen planus, depicting these individuals as highly strung and overconscientious, with a tendency to worry excessively. Studies reported since Wilson's original documentation suggest anxiety and stress as factors contributing to the disease and subsequent recurrence of lichen planus. The disorder is a chronic, inflammatory mucocutaneous disease of unknown etiology. Lichen planus behaves like a cell-mediated immune response (type lV hypersensitivity reaction), but in the past few years, lichen planus has been classified by some as an autoimmune-related disease. Since an antigen has not been discovered to make lichen planus fit soundly into the autoimmune category, some argue that it is premature to classify it as autoimmune. The debate goes on. Controversy exists among researchers, educators, and practitioners about the malignancy potential of lichen planus as well. Some researchers believe that any chronic lesions have the potential to transform into malignancy given time and the degree of erosion (Eisen, 2002). Some researchers suggest that there is a high degree of misdiagnosis initially with regard to oral lichen planus (Lodi et al., 2005) and a failure to diagnose lichen planus in other areas of the body such as the esophagus (Fox et al., 2011), vagina (Edwards, 2010), and skin (Stojanovic et al., 2011). The disease may be labeled lichen planus but may be premalignant or malignant from the original diagnosis. This is usually due to relying on a clinical diagnosis rather than a tissue biopsy diagnosis. Additionally, the disease may begin as lichen planus and be followed with that diagnosis, but at some point, lesions become dysplastic or cancerous. The disease can appear similar to other mucosal diseases, and a careful diagnosis is crucial. A biopsy and immunofluorescence are needed for a definitive diagnosis.

Method of Transmission: Lichen planus is not a contagious disease. It cannot be transmitted to other individuals.

Epidemiology: Lichen planus affects approximately 0.5 to 2.5% of the population. Lichen planus usually occurs in midlife, at an average age of 57. However, reported cases have been documented in children and in the elderly. There is a female predilection, with reported figures ranging from 57 to 75%. A total of 48% of females are postmenopausal or posthysterectomy. Approximately 25% of lichen planus occurs with external skin lesions in conjunction with the oral lesions. Since many patients are on medications and may actually have what is termed **"lichenoid" reactions** that are reactions to medications and allergy to various products, this number may be often mixed with true lichen planus. Allergic reactions to metals, fragrances, and preservatives may promote more contact-type allergies as well (Torgerson et al., 2007). Figure 13.8 depicts a cutaneous lesion of lichen planus with purple papules and keratotic areas.

Pathogenesis: Lichen planus is often overlooked by practitioners and confused with other lesions, since its appearance

APPLICATION 13.1

Areas of discoloration in the mouth and lip area are commonly observed in patients within a dental practice. The clinician must sort out the causes of these lesions and suggest a course of action. Sometimes, the possibilities are numerous, and using a systematic technique to question the patient is very helpful in determining the cause of the lesion.

1. If the patient is new, a complete health history is essential.
2. If the patient is a maintenance patient, an updated history is needed.
3. Be specific in identifying the lesion by showing the patient where the lesion is located.
4. Open a dialogue regarding the possibilities in etiology.
5. Determine whether the lesion is vascular or nonvascular.
6. Determine whether the patient has noticed the lesion:
   a. Ask when the person first noticed the area in question.
   b. Ask how long he or she believes the lesion has been present.
   c. Ask about relevant events that may have occurred at that time, such as a fall.

By involving the patient, the lesion can often be identified quickly, and the issue can be resolved with suggestions on how to avoid future injury. Injury that cannot be identified may require further tests. Intraoral photographs are priceless in documenting lesions and crucial for any follow-up evaluations. Refer to Clinical Protocol #26 on Helping Relationships for the Dental Hygienist and #27 on Motivational Interviewing.

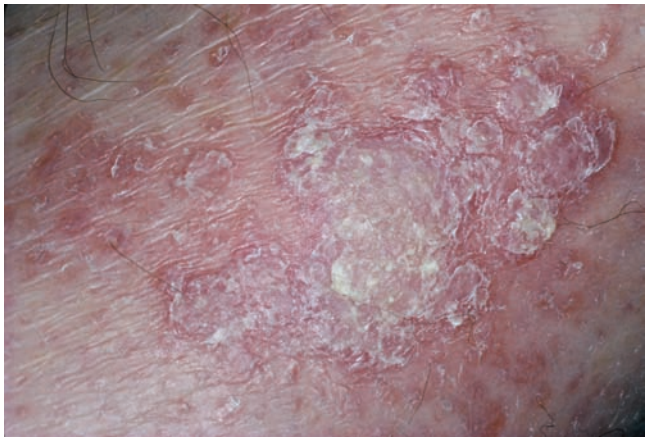

FIGURE 13.8. Cutaneous lichen planus on the arm of a patient. (Courtesy of Dr. Sumner Sapiro.)

FIGURE 13.9. Bullous oral lichen planus. (Courtesy of Dr. Terry Rees.)

can have many forms. It is known to occur and then go into a remission state for periods of time, only to recur later. There are various forms of oral lichen planus; some of the lesions are white, some are red, and some have a mixture of colors. For this section, since we are studying red lesions, we concentrate on forms that have a red appearance. The white lesions associated with lichen planus are discussed in Chapter 14. Andreasen (1968) divided lichen planus into six clinical forms. The classification includes reticular, papular, plaque-like, atrophic, erosive, and bullous types. Some researchers report an increased relationship between lichen planus and hepatitis C. Most of the increases in hepatitis have been reported in European countries (Carrozzo et al., 2002) such as Italy. Lichen planus occurs most frequently on the buccal mucosa (about 90% of the cases), followed by the tongue (30%) and gingival and alveolar ridge (13%). The lips, palate, and vermillion border are rarely seen (Scully et al., 1994).

Extraoral Characteristics: Cutaneous lesions of lichen planus present as keratotic, **violaceous**, pruritic plaques occurring most frequently on the flexor surfaces in 30 to 50% of patients. Lesions of the genitalia are present in approximately 2% of patients with lichen planus, resulting in painful erosions of the vulva and vaginal areas of women known as vulvo-vaginal-gingival syndrome (Eisen, 1994; Pelisse, 1989). However, often no connection is made between the oral and genital symptoms by either dental or medical practitioners. The patient should be advised to let her gynecologist know that she has oral lichen planus so that she may be evaluated for genital lesions as well. Pineal and rectal lesions sometimes occur in patients with lichen planus, and the nail beds are sometimes involved, resulting in scarring of the fingernails and toenails (Edwards, 2010).

Perioral and Intraoral Characteristics: Patients will exhibit either one or a combination of several forms of lichen planus, which are classified as reticular, plaque-like, papular, erythematous or atrophic, bullous, or erosive–ulcerative.

- The reticular form of lichen planus is the classic form, and the lesions exhibit white striae called Wickham striae. This form is discussed in Chapter 14.
- The papular form is discussed in Chapter 14.
- The plaque form resembles leukoplakia and is discussed in Chapter 14 as well.
- The atrophic form appears as red patches with very fine white striae. This form often appears on the gingiva, with varying patterns of redness and striae.
- The bullous form of lichen planus ranges from a few millimeters to centimeters in diameter and is not usually seen clinically since the vesicles usually rupture rapidly. However, this form may present with several of the specified types of oral lichen planus. Figure 13.9 depicts a bullous lichen planus lesion with erythematic tissue surrounding the bulla.
- Erosive forms can be very painful. The erosive form has been associated with increased malignancy, and chronic forms of this type should be carefully monitored with biopsies when changes occur. The lesions may be raw, red, and ulcerative, with pseudomembranous coverings. This form is often referred to as desquamative gingivitis, which is a general term for several mucosal disease states. Figure 13.10 shows erosive lichen planus with a pseudomembranous covering. Figure 13.11 also shows an erosive form of lichen planus.

Often, a combination of forms is seen clinically. Another lesion associated with oral lichen planus and, unfortunately, very difficult to differentiate is what is termed a **lichenoid reaction.** If the lesion is a lichenoid reaction to a product, removal of the product usually causes the lesion to dissipate. Figure 13.12 depicts a reddened area opposite the molar area that is a lichenoid reaction to amalgam. Lichenoid reactions to dental materials occur in the area of contact with the tissue. In this case, the reddened area is opposite an amalgam buccal restoration (Rees, 2011).

Esophageal lichen planus is reported with **dysphagia** (difficulty in swallowing) resulting from esophagitis and stricture formation. Esophageal lichen planus sometimes

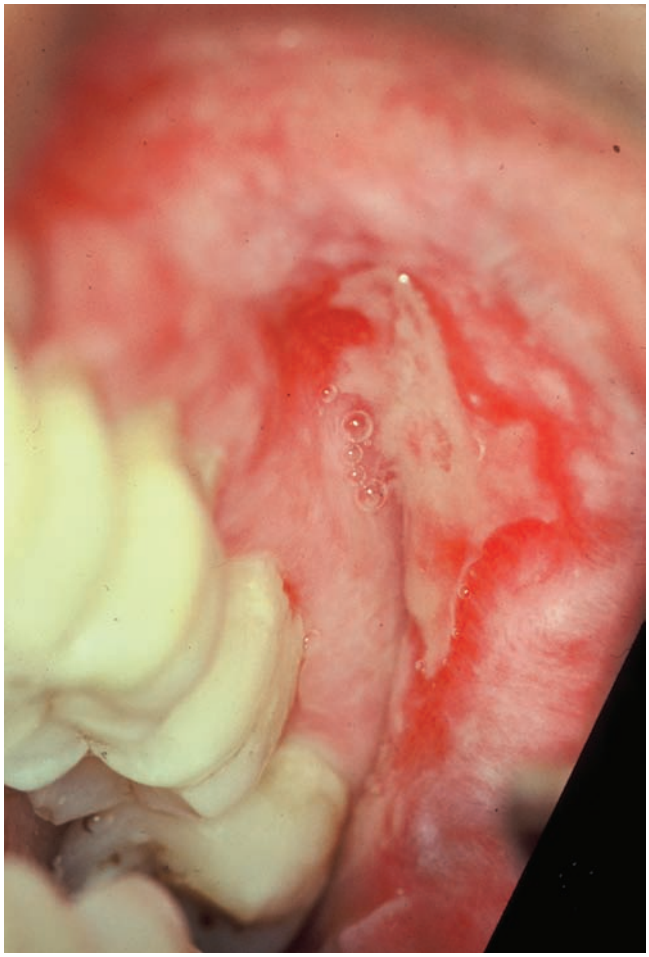

FIGURE 13.10. Erosive oral lichen planus. (Courtesy of Dr. Terry Rees.)

occurs after oral lichen planus has been diagnosed, and sometimes, patients complain about throat sensitivity without a definitive diagnosis being made. Physicians should be made aware of oral lichen planus and the patient should be evaluated for other forms in other areas of the body (Fox et al., 2011).

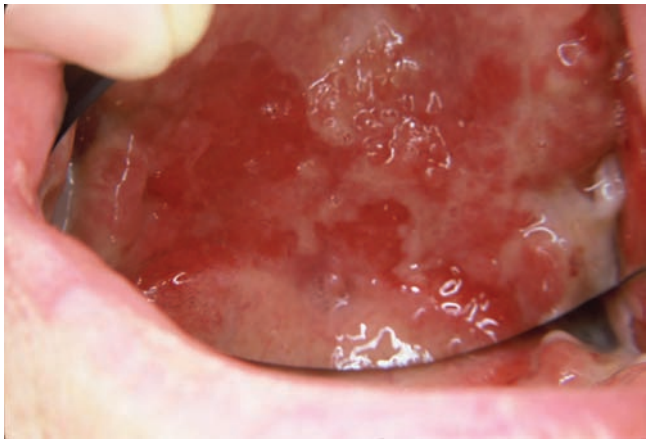

FIGURE 13.11. Erosive oral lichen planus. (Courtesy of Dr. Sumner Sapiro.)

FIGURE 13.12. Lichenoid reaction.

Distinguishing Characteristics: One of the characteristics of lichen planus is Wickham striae, which appear as a lacy, white pattern that resembles the lichen-type moss that is often seen on rocks (see Chapter 14). Additionally, lesions associated with lichen planus are usually purple, pruritic, polygonal papules when on the skin surface. Although the color varies, lichen planus is usually described with these terms (see Fig. 13.8).

Significant Microscopic Features: The tissue exhibits liquefaction and degeneration of the basal cell layers and an increase in lymphocyte infiltrates. The basal cell layer typically has a bulbous or "sawtooth" appearance. Degenerating epithelial cells, or **Civatte bodies**, are observed. Civatte bodies, observed microscopically, are eosinophilic ovoid bodies that are apoptotic (dying cells) or necrotic keratinocytes (epithelial cells that ultimately keratinize) at the basement membrane.

Dental Implications: Establishing a home regimen that works for the individual patient is important. Professional scaling and a prophy are essential in limiting the frequency of lesions. Home care products that cause minimal abrasion and have low amounts of flavoring agents are best for lichen planus lesions, and a soft-bristle brush is recommended. The patient may react to a dental product such as amalgam or the materials of a gold crown. The reaction may be what is termed a "lichenoid reaction." The tissue in contact with the product will resemble lichen planus. Offending products include certain medications, and the patient may have a generalized erythematous appearance similar to lichen planus. Often, removal of the material or changing to another class of medication alleviates the problem. It is even difficult to differentiate the lichenoid reaction from true lichen planus histologically. Maintenance appointments at regular intervals with as little disruption to the tissue as possible are important for patients with mucosal disease. Air polishers are not recommended, and scaling with hand instruments is necessary in those with highly erosive lesions (see Clinical Protocol #3). High settings on ultrasonic instruments may cause tissue trauma.

Differential Diagnosis: Some considerations may be:

1. Lupus—Chapter 12
2. Benign mucous membrane—Chapter 11
3. Pemphigoid—Chapter 11
4. Pemphigus vulgaris—Chapter 11
5. Squamous cell carcinoma—Chapters 5 and 12
6. Lichenoid reactions—Chapter 13

Treatment and Prognosis: Depending upon the patient, the disorder can be lifelong, but some patients can have one episode of oral lichen planus and not have any oral lesions again. Essentially, the disease is described as unpredictable. Because the condition has periods of remission and recurrence, many dental practitioners become frustrated with a lack of finality and progress. Since there is an increased risk of malignancy, the patient should be carefully monitored long-term, and any changes in the tissue must be noted. Intraoral photographs are helpful in evaluating subtle tissue changes. There may be a need for increased biopsy, depending upon the changes. For mild, reticular forms, usually no treatment is needed. However, if the lesions become ulcerated or changes in form are noticed, a corticosteroid is usually prescribed for treatment. Even if treatment is not needed, long-term follow-up and monitoring are required because of the possibility of oral cancer.

The usual medications that are prescribed include fluocinonide, betamethasone (Diprolene) 0.05%, and clobetasol propionate (Temovate) 0.05%. These medications have been found effective in the treatment of lichen planus (see Clinical Protocol #2 on applying topical corticosteroids). Patients often have trouble getting the topical corticosteroids to remain in place long enough to be effective treatment. Sometimes, with the erosive forms, intralesional corticosteroid injections may be beneficial. *Candida* (see Clinical Protocol #5) is often a problem when corticosteroids are prescribed for extended periods, and the patient may need periodic treatment for *Candida* with antifungal medications. (See Clinical Protocol #6 for the recall guidelines for mucosal diseases.)

NAME: Hypersensitivity reactions

Etiology: **Hypersensitivity** reactions appear to be delayed cell-mediated immune responses. Cell-mediated immune response is not the classic type 1 response that is associated with angioedema (see Chapter 4). Hypersensitivity is edema of the subcutaneous tissue such as wheals, also known as hives or welts. Several varieties of contact allergies are known that affect the oral tissues and are considered orofacial disorders. **Plasma cell gingivitis** and allergic gingivostomatitis are terms that are associated with allergic responses to substances. Contact allergies and sensitivity to food products, flavoring agents, dental hygiene products, and even dental restorative products are all reported in the literature as causes. With more and more flavoring agents and combinations of products used by patients, increased numbers of cases are being reported and recognized as contact allergies. Additionally, orofacial granulomatosis that features noncaseating epithelioid granulomas in the lamina propria is reported in association with sodium benzoate and tartrazine additives in red wine, additives found in food products such as monosodium glutamate, and cinnamic aldehyde (Endo & Rees, 2006). The lips and face may become swollen. The gingiva is the prime area of involvement. Additionally, the buccal mucosa and tongue may appear enlarged, with folding leukoplakia (white-appearing tissue). A fiery red gingiva is characteristic of a hypersensitivity reaction and involves granular surface changes. Contact allergies are usually associated with dental products (Rees, 2011), such as toothpaste and mouth rinses, and specific foods, such as cinnamon, wheat, dairy products, chocolate, eggs, and peanuts. Many of the colas contain cinnamic aldehyde as do chewing gums, especially the red colored ones. Some patients react to the ingredients found in toothpaste and the antitartar ingredients in tartar-control toothpaste with redness and sloughing. Ingredients, such as cinnamic aldehyde and cinnamon oil, and the preservatives, such as benzoic acid, sodium benzoate, and methyl paraben, are usually the cause of sensitivity to toothpaste (see Clinical Protocol #6).

Method of Transmission: The red lesions and erythematic tissue are localized and not contagious.

Epidemiology: The responses to specific allergens can occur at any age and affect both sexes equally.

Pathogenesis: A type lV hypersensitivity reaction is produced (see Chapter 4).

Extraoral Characteristics: Hypersensitivity reactions may be external skin reactions as well as intraoral tissue reactions. Chapter 23 discusses some of the external skin reactions. With oral contact hypersensitivity reactions, the lips and the inner wet tissues may also be involved.

Perioral and Intraoral Characteristics: The gingiva appears fiery red and somewhat bulbous. Figure 13.13 shows the gingival tissue of a patient with cinnamic aldehyde allergies before and after discontinuing cinnamon products.

The patient in Figure 13.13A was using multiple products with cinnamon, including soda, toothpaste, chewing gum, mints, and mouth rinses. In this photo, a classic feature of the contact allergy is the clearing above the deeply red gingiva. This clearing indicates that the tissue is contacting the irritant up to this point, suggesting that a toothpaste or consumed product is responsible. Because the lip is folded over the vestibule, this clear area is protected from the offending product, while other adjacent tissue is bathed in the product.

Distinguishing Characteristics: Allergic-type tissue responses in the mouth related to dental products have a velvety red appearance with distinctive clearing in areas where products do not contact the tissue. One such area is the oral vestibule, which is protected by the overlying tissue found in this area (Scully, 2006; Rees, 2011).

FIGURE 13.13. **A.** Cinnamic aldehyde allergy. **B.** Tissue after discontinuing cinnamon products. (Courtesy of Dr. Terry Rees.)

Significant Microscopic Features: The key feature of the allergic response is plasma cells. The morphology is normal. The epithelium exhibits **spongiosis** (inflammatory intercellular edema of the epidermis) and inflammatory cells.

Dental Implications: With any red, blue, or purple lesion, the underlying cause must be found. The dental implications consist of determining the source and discontinuing contact with the offending products.

Differential Diagnosis: The practitioner would want to consider the following:

1. Lichen planus—Chapter 13
2. Lupus—Chapter 12
3. Benign mucous membrane pemphigoid—Chapter 11
4. Pemphigus vulgaris—Chapter 11
5. Squamous cell carcinoma—Chapter 12
6. Vitamin deficiency and anemia. When the tongue is involved in an allergic response, the fissuring and cobblestone effect may resemble that of a vitamin deficiency or anemia—Chapter 9
7. Crohn disease—Chapters 10 and 12
8. Sarcoidosis—Chapter 23
9. Foreign body reaction—Chapter 3
10. Deep mycotic infections—Chapter 12

Treatment and Prognosis: The correct diagnosis of the offending product or allergen is often through trial and error. The patient may discontinue the use of or contact with the agent, and the tissue is then evaluated again after a period of time. In the case of toothpaste and food allergy, a tissue response is usually evident within 2 weeks. Prognosis is excellent when the hypersensitivity agent is identified and its use is discontinued.

Infections

Infections that occur in the mouth have many different appearances, such as redness, white tissue, raised, eroded, and ulcerated. Infections may mimic other types of disease states, so providing a correct diagnosis is crucial. As described in previous chapters, fungal, bacterial, and viral lesions cause the tissue appearance to vary, depending upon the location and the type of agent present. This discussion involves those types of infections that may appear red or purple. *Candida* is discussed next because it is a fungal infection that exists and is commonly observed in patients—especially those on certain medications. The appearance of oral *Candida* is varied, with erosive lesions of both red and white patches occurring orally. Specifically, the red lesions are discussed in this chapter; the white lesions related to *Candida* are discussed in Chapter 14.

NAME: Candidosis (candidiasis)

Etiology: Candidosis, often referred to as candidiasis, is a fungal infection caused by species of the genus *Candida*. *C. albicans* is the principal species associated with the oral infection. It is the most common fungal pathogen (Abraham, 2011). The fungus inhabits the gastrointestinal tract, the mouth, and the vagina. When the body systems are in harmony and the host is at an optimal level, the organism is not a problem. However, certain individuals may be more prone to the overgrowth of *Candida* than others, such as those in immunocompromised states of health, individuals taking certain medications, patients using corticosteroids that may alter the immune system, and patients taking antibiotics for various conditions. Any time there is a disturbance in the normal bodily flora, an individual may be susceptible to developing a candidal infection. Endocrine disturbances and xerostomia predispose a person to the likelihood of developing *Candida* infection. The greater and more severe the candidiasis in this group of patients, the more difficult it is to manage the recurrence of the organism.

Method of Transmission: *Candida* is not transmitted to another individual unless that person is susceptible as well. HIV and AIDS patients are especially vulnerable to the organism. Patients undergoing chemotherapy and radiation treatment are also more susceptible to *Candida* because of reduced immune system function.

Epidemiology: Pseudomembranous forms are found more in the elderly and young infants, while the erythematic forms are found more often in adults wearing dentures and appliances. There is an equal predilection of males and females.

Pathogenesis: *Candida* infections are usually superficial, but they can become deep fungal infections that affect the brain, heart, eyes, and kidneys when the individual is immunocompromised. Individuals who are taking antibiotics for extended periods of time destroy all of the "good" bacteria (organisms that compete with *Candida*), thereby allowing the unwanted *Candida* to become more numerous. Normally, *Candida* is kept in check within the body, but at times such as in the use of antibiotic therapy, the organisms may become more numerous. Individuals who are on antibiotics and those who may be in a debilitated state are more susceptible to oral *Candida. C. albicans* thrives in warm, moist areas, and certain conditions may make the host more prone to increased levels of the organisms. This is especially true for patients who are using corticosteroids for oral conditions such as lichen planus and other mucosal disorders in which inflammation is a key factor. Certain medical conditions predispose the patient to development of *Candida*, such as immunocompromised states, diabetes, hypoparathyroidism, and certain blood disorders. These conditions may make a person more vulnerable to *Candida* and in some cases may have a genetic component to the development of *Candida* related to certain diseases. Generally, any health condition that causes a debilitated state would make persons more susceptible to *Candida*. Refer to Box 13.1 for a listing of the more common predisposing factors associated with candidosis.

Extraoral Characteristics: *Candida* is often found in elderly patients and is sometimes due to the loss of teeth and sagging tissue at the commissures. The loss of dimension at the commissures is a common problem in aging and this area may sag and allow saliva to accumulate in the folds. Damp tissue at the commissures is a prime condition for *Candida*. The general health of the elderly, decreased immune function, and poor dietary practices predispose patients to *Candida* infections. Other areas in the body are also prone to *Candida* such as the esophageal and vaginal tissues.

Perioral and Intraoral Characteristics: As mentioned above, *Candida* can have several different appearances. *Candida* may have a white appearance (pseudomembranous type) as well as a red color (erythematous type), depending upon the location and predisposing factors. *Candida* that appears white is discussed in more detail in Chapter 14 under white lesions. The white acute type of *Candida* infection (sometimes called thrush) may appear plaque-like or cottage cheese–like and usually is found in the pharynx, the tongue, and buccal mucosa as well as the mucosal folds. These lesions may be wiped off, and the surface that remains may appear red, raw, and ulcerative. The raw appearance may be clinically evident, however, a solid white appearance may occur as well and this type is discussed fully in Chapter 14. The erythematous type has a bright red appearance. The chronic erythematous type is commonly found in denture wearers, with the usual sites being under the denture and on ridges. *Candida* may cause symptoms such as burning, and if xerostomia is involved, the patient may complain of dryness with changes in taste sensations. Figure 13.14 depicts erythematous tissue with pseudomembranous areas covering the gingiva.

BOX 13.1 Predisposing Conditions Associated with Oral Candidiasis

- Immunocompromised patients
  - Elderly or very young age
  - Cancer therapy
- Long-term corticosteroid therapy
  - Cushing syndrome
  - Treatment for mucosal diseases such as lichen planus, pemphigoid, pemphigus, lupus
- Endocrine candidiasis syndrome
  - Diabetes
  - Hypothyroidism
  - Hypoparathyroidism
  - Hypoadrenocorticism (Addison disease)
  - Hyperadrenalism
- Vitamin deficiencies
  - Malnutrition
- Medications
  - Antibiotics
  - Corticosteroids
  - Oral contraceptives
- Blood disorders
  - Anemia
  - Leukemia
- Genetic
  - Congenital
- Appliances
  - Dentures
  - Decreased vertical dimension
  - Poor hygiene practices
  - Partials
  - Retainers
- Oral environment
  - Poor oral hygiene
  - Xerostomia
  - Stress
- Hormonal fluctuations
  - Pregnancy
  - Menopause

FIGURE 13.14. Erythematous *Candida*. (Courtesy of Dr. Michael Brennan.)

FIGURE 13.15. Partial denture stomatitis.

Candida may be found in various locations in the oral and perioral tissues. The recognition may lead to a diagnosis of the following types of Candida-related states:

- Pseudomembranous candidiasis—discussed in Chapter 14
- Chronic hyperplastic candidiasis—discussed in Chapter 14
- Erythematous candidiasis—may arise due to chronic pseudomembranous candidiasis and is also strongly associated with HIV infection; this form appears as a red erythematous tissue.
- Acute atrophic candidiasis—associated with broad-spectrum antibiotics; the patient may complain of a burning sensation and the tongue will have a red appearance.
- Chronic atrophic candidiasis (denture stomatitis)—diffuse erythematic lesions found under and around a denture, partial denture, or prostheses; Figure 13.15 shows *Candida*-infected red tissue observed under a denture.
- Angular cheilitis (also referred to as **perlèche)**—lesions are found at the commissures and appear red, dry, and rough; angular cheilitis lesions may occur in conjunction with oral *Candida*. Figure 13.16 shows angular cheilitis at the commissure, and the patient has an extremely dry mouth.

FIGURE 13.16. Perlèche. (Courtesy of Dr. Terry Rees.)

FIGURE 13.17. Median rhomboid glossitis. (Courtesy of Dr. Doron Aframian.)

- Median rhomboid glossitis—once thought to be a developmental defect of the tongue, recent studies now suggest a relationship between *C. albicans* and median rhomboid glossitis. Papillary atrophy is characteristic in the rhombus-shaped, well-demarcated, central denuded area of the tongue with a red appearance. Median rhomboid glossitis is also described as hyperplastic candidiasis. Figure 13.17 depicts median rhomboid glossitis in the center part of the tongue, forming rhomboid-shaped lesions.

Distinguishing Characteristics: The white cheesy pseudomembranes associated with the pseudomembranous type can be wiped away to expose an erythematic, raw, denuded area.

Significant Microscopic Features: Many fungal hyphae are the prime diagnostic feature. Figure 13.18 depicts the histology of *Candida* with hyphae demonstrated.

Dental Implications: Common dental manifestations related to candidiasis include xerostomia (see Clinical Protocol #4) and poor oral hygiene. Optimal treatment emphasizes home care and compliance with procedures focused on treating existing *Candida* to ensure that the patient is not reinfected.

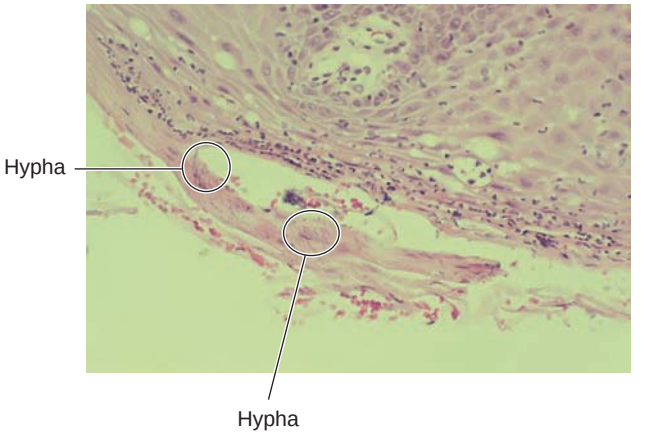

FIGURE 13.18. Histology of a lesion with *Candida* and hyphae.

Differential Diagnosis: Diagnosis is usually based on microscopic examination of the tissues and membrane scrapings are placed in KOH solution (see Clinical Protocol #5). *Candida* hyphae are seen microscopically, and cultures may provide counts of the organisms. Since *Candida* can appear both white and red, the clinician must consider other possible lesions as well. Some considerations for red lesions include the following:

1. Lichen planus—Chapters 13 and 14
2. Lupus—Chapter 12
3. Pemphigus—Chapter 11
4. Pemphigoid—Chapter 11
5. Lichenoid reactions—Chapters 13 and 14
6. Squamous cell carcinoma—Chapters 5 and 12

Treatment and Prognosis: The treatment of choice is nystatin oral suspension and statin oral powder, and clotrimazole oral troches. Medications for angular cheilitis include nystatin ointment, miconazole cream (2%), and clotrimazole (1%). Reinfection can occur if appliances, toothbrushes, and dentures are not treated along with the infected person. The *Candida* organisms on the devices can reinfect the patient. Disinfection of oral appliances can be accomplished via the use of chlorhexidine and nystatin solution (2% chlorhexidine gluconate, Peridex). Cases have been reported in which partners who are both prone to *Candida* continue to reinfect each other. See Clinical Protocol #5 for information on how to manage *Candida* infections. The prognosis depends on the health state of the patient.

Neoplasms

The terms **neoplasm** and tumor are used interchangeably and are classified as either malignant or benign. Benign neoplasms may vary in size and usually do not cause problems unless they begin to interfere with other tissues or organs. Malignant neoplasms do cause problems and also have the potential to spread to other parts of the body. They need to be surgically removed and may require adjunctive treatment with radiation or chemotherapy. Oncology is the study of tumors and their treatment.

NAME: Kaposi sarcoma

Kaposi sarcoma is a malignant neoplasm occurring in the skin, oral tissues, and lymph nodes. The neoplasm is more common in patients who are in debilitated states such as those with AIDS and the elderly. Human herpesvirus 8 is associated with this sarcoma, and depending upon the stage, it may appear as a minor lesion. This tumor is discussed fully in Chapter 22. The lesions are mentioned here because of their blue-to-purple hue. (Figure 13.19 shows the blue and bruised appearance of Kaposi sarcoma opposite 3, 4, and 5 in the palatal region.) The hard palate and gingiva are most often affected. Early lesions occur as nonpainful, purple-to-red macules that may be focal or diffuse and are easily overlooked.

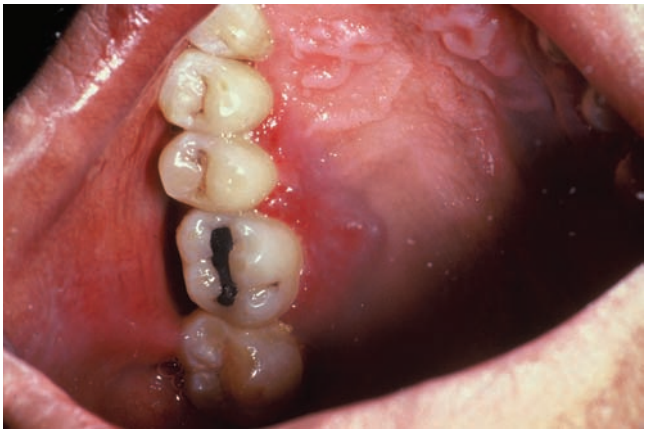

FIGURE 13.19. Kaposi sarcoma. (Courtesy of Dr. Michael Brennan.)

NAME: Erythroplakia (erythroplasia)

Etiology: The term **erythroplakia** refers to a *red patch* on oral mucous membranes. Erythroplakia encompasses several variations of both velvety red lesions and, sometimes, those containing a mixture of red and white lesions, which is referred to as **speckled leukoplakia** or **erythroleukoplakia** (discussed in more detail in Chapter 14). An increased incidence of erythroplakia is associated with tobacco and alcohol use. Dietary deficiencies and lifestyle factors may also be responsible in some cases. Additionally, chronic friction and exposure to irritants producing chronic inflammation are known to be sources.

Method of Transmission: The lesion is not contagious.

Epidemiology: Erythroplakia lesions have a high rate of progressing to oral cancer, with most having dysplastic changes in the cells. At least 85% are usually severely dysplastic or frank malignancy (Scully, 2005). Incidence of malignant and premalignant lesions appears to increase after age 50, and as with all oral malignancy, there is a male gender predilection. The usual sites for erythroplakia are the floor of the mouth, the soft palate, and the buccal mucosa.

Pathogenesis: Erythroplakia is a generalized term that encompasses red, red and white, and variations of red and white lesions. The term *erythroplakia* is used to describe a lesion that is usually premalignant and occurs throughout the mouth. Leukoplakia (white lesions), which is more common than erythroplakia, is discussed in Chapter 14. When the epithelial cells no longer produce keratin (white lesions), they may undergo cellular changes and are more susceptible to malignancy, progressing to a more erythroplakic form. Although white lesions can be malignant, the percentage of malignancy is greater with erythroplakia, or red lesions.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: Erythroplakia lesions may have a velvety red color or be dark pink. The surface areas are varied, sometimes appearing corrugated/pebbly and in some instances very smooth. The lesion may be

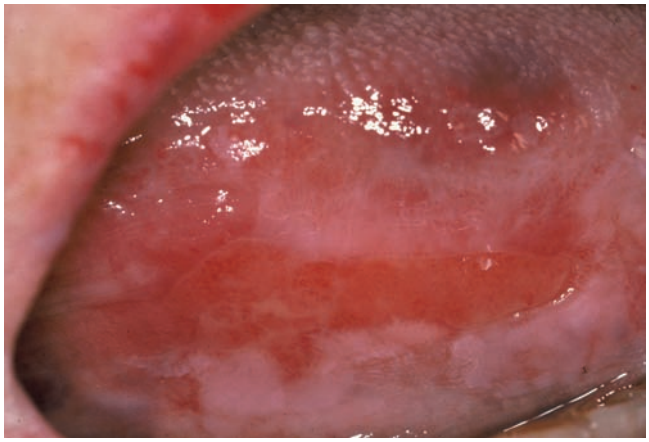

FIGURE 13.20. Erythroplakia. (Courtesy of Dr. Terry Rees.)

broad and coalescing or it may be circumscribed and localized. Essentially, erythroplakia, along with squamous cell carcinoma (SCC), has many appearances. Figure 13.20 depicts the lateral border of the tongue with a velvety, reddened area that was found to be dysplasia. This lesion may be classified as erythroplakia. The lesions are often interspersed with lighter areas, representing keratosis. The lesions may be indurated (hardened) or they may be soft when palpated.

Distinguishing Characteristics: Deep, velvety red tissue is a distinguishing characteristic of this type of lesion.

Significant Microscopic Features: The lesions are considered premalignant and the earliest form of cancer. Approximately half of erythroplakias are cancerous. Most show severe dysplastic changes, and increased vascularity accounts for the red color of tissue.

Dental Implications: Erythroplakia-type lesions should be assessed for cancer cells via biopsy when warranted. However, the dilemma for the clinician is often *when* to biopsy the lesion, as he or she may have some concerns but not enough to warrant a biopsy. Any lesion should be guarded, watched carefully, or biopsied. In the initial evaluation, if an area of concern is detected, the clinician may want to use one of the abnormal cell detection devices. These devices detect questionable cells or abnormal tissue responses. One technique is the brush biopsy; another such device uses a rinse/light apparatus to detect cellular abnormality. See Clinical Protocol #12 for types of assessments and tests that may be used. Recent positions on the use of tests and clinical assessments conclude that these devices are *adjuncts* to the correctly performed clinical head and neck exam (Rethman et al., 2010). When a cause cannot be determined or the clinician is concerned about the clinical characteristics, a referral for a biopsy should be made. Also, any lesion that does not subside after 2 weeks warrants a biopsy. Additionally, if some abnormality is detected when using the brush biopsy or other abnormal cell detection devices, a biopsy should be performed.

Differential Diagnosis: Considerations are:

1. Squamous cell carcinoma—Chapter 12
2. Kaposi sarcoma—Chapter 22
3. Systemic lupus erythematosus—Chapter 12
4. Lichen planus—Chapter 13
5. Pemphigoid—Chapter 11
6. Pemphigus—Chapter 11
7. Vascular-appearing lesions—Chapter 13
8. Hypersensitivity reactions—Chapter 13
9. Erythematous candidiasis—Chapter 13

Treatment and Prognosis: Treatment depends upon the histologic diagnosis. Any dysplastic areas are excised, depending upon the site, type, and results of the erythematous lesion biopsy. In some cases, radiation and chemotherapy are used. It is suggested that follow-up for any potentially malignant lesion be performed at 1-, 3-, 6-, and 12-month intervals.

Vascular Malformations

Malformations of capillaries, veins, arteries, or lymph vessels are considered **vascular malformations**. These malformations can be congenital (that is, occurring at or around birth), or they can be acquired (presenting later in life).

NAME: Varicosity (varix)

Etiology: The varicosity, or varix, is an abnormally dilated and tortuous vein that is an acquired vascular malformation. Varices (plural of *varix*) are found under the tongue (referred to as **lingual varicosities**) and sometimes are highly visible in older adults. The varicosity is thought to be a developmental abnormality and not associated with any systemic disease states. However, some association exists between varicosities found orally and those found in the legs of adults.

Method of Transmission: This is a localized lesion with no transmission factor.

Epidemiology: Varicosities are found in adults over 60 years of age; they are rare in children. There is an equal predilection for males and females.

Pathogenesis: Varicosities indicate a weakness in the vessel wall. Since they are normally found in adults and not in children, they are associated with the aging process.

Perioral and Extraoral Characteristics: Some reports indicate a connection between enlarged veins in the legs and lingual varicosities. **Thrombosis blood clots** can occur in these lesions, and if this does occur, the lesion will be firmer on palpation. The formation of thrombosis is rare. Assessment of a thrombosis of the varicosity is needed in most cases when suspected during palpation. Sometimes, in older adults, the enlargement is found on the lower lip and is referred to as a **venous varix** (singular or solitary). The vessel wall becomes weak from chronic sun exposure. Figure 13.21 depicts a venous varix on the lower lip.

FIGURE 13.21. Varix.

Intraoral Characteristics: The veins appear dark blue to purple and may be found on the lingual surface of the tongue, lips, or buccal mucosa. The practitioner may determine whether the lesion is vascular by compressing and releasing the area in question **(diascopy)** to determine blood flow and to differentiate between a vascular and nonvascular lesion. The varicosity that occurs under the tongue is termed lingual varix or lingual varocosity. Figure 13.22 is representative of lingual varicosities (see Box 13.2).

Distinguishing Characteristics: The blood supply is disrupted by compression and resumes with release. A thrombus may be apparent in some cases and will seem firm when palpated.

Significant Microscopic Features: Not applicable

Dental Implications: There is no specific dental implication other than the appearance of the varicosity. Some patients object to the appearance of varicosities when they appear on the more visible areas such as the lip.

FIGURE 13.22. Lingual varicosity.

BOX 13.2 Hemorrhages and Varicosities

Entity	Size	Color	Blanch with Diascopy
Petechiae	Pinpoint 1 to 2 mm	Pink/red	No
Purpura	Larger than 2 mm to 1 cm	Dark pink/red	No
Ecchymoses	Larger than 1 cm	Red/purple Yellow/green with age	No
Hematoma	Vary in size	Dark red/blue	No
Lingual varicosity	Vary in size	Dark blue	Yes
Venous varix	Vary in size	Dark red/blue	Yes
Hemangioma	Vary in size	Dark red/blue	Yes
Lymphangioma	Vary in size	Red/blue/clear	Yes
Telangiectasia	Usually small in size and thread-like	Red, red-brown	Yes

The entities above will appear in varying colors depending upon the location, age of the wound or injury, and the state of tissue repair. For example, a palatal ecchymosis may be caused by the patient using an object to induce vomiting while purging. This will dissolve as the body absorbs the pooled blood when the behavior is discontinued.

Differential Diagnosis: Other lesions to be considered are:

1. **Hematoma**—Chapter 13. The hematoma is not a vascular lesion. When pressure is applied, hematomas do not blanch, since they are an accumulation of blood in a specific area of the tissue, usually due to trauma. Figure 13.23 depicts a hematoma on the ventral surface

FIGURE 13.23. Hematoma.

of the tongue. The use of diascopy is helpful in determining whether the lesion will blanch upon pressure since hematomas may be confused with the hemangioma.
2. Hemangioma—Chapter 13
3. Lymphangioma—Chapter 13

Treatment and Prognosis: The varicosity requires no treatment unless it occurs in areas such as the lip or buccal mucosa and is of concern cosmetically to the patient. Formation of a thrombus warrants surgical removal. The prognosis is excellent.

NAME: Congenital hemangioma (strawberry nevus)

Etiology: **Hemangioma** is one of the most common lesions in the mouth and is a benign proliferation of blood vessels, found in infancy and childhood. It consists of benign neoplasms composed of capillaries and venules. The hemangioma is a congenital entity usually present at birth, or it may be acquired through trauma in adulthood. The hemangioma is not a true neoplasm but may be a **hamartoma** or malformation. A hamartoma is a focal malformation consisting of an abnormal mixture of tissue elements or an abnormal amount or proportion of a single element normally present within a specific site.

Method of Transmission: The lesion is localized and is not contagious.

Epidemiology: Although hemangiomas are found throughout the body, they tend to have a higher rate of occurrence in the head and neck region. They are found in approximately 2% of infants and are found more frequently in females. By age 2, 10% of the population exhibits a hemangioma with **involution** (return of an enlarged organ to normal size) occurring. The areas in which hemangiomas seem to occur more frequently are the tongue, lips, and buccal mucosa. Hemangiomas may be found in any soft tissue areas or bony intraoral locations.

Pathogenesis: Unlike neoplasms or tumors, the hemangioma does not exhibit unlimited growth. Many will dissipate, while others remain throughout life. When the lesions occur in adults, they are most likely the result of localized trauma and may be considered reactive lesions in these cases. The prime areas of trauma are the most susceptible sites such as the lip and tongue.

Several classifications of hemangiomas are noted, but the two most widely encountered are:

1. Capillary hemangiomas involving smaller capillaries, the most widely occurring type.
2. Cavernous hemangiomas that contain larger blood vessels, termed the cavernous type.

Extraoral Characteristics: Depending upon the location and depth of the hemangioma, the color will vary from a dark pink in the deeper tissue areas to dark purple in superficial areas. The lesions may be single or multiple. Figure 13.24 shows a capillary hemangioma of the face.

FIGURE 13.24. Hemangioma. (Tasman W, Jaeger E. The wills eye hospital atlas of clinical ophthalomology. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2001.)

Perioral and Intraoral Characteristics: The intraoral hemangioma usually appears as a deep blue to red enlargement, with a raised appearance. Figure 13.25 depicts a lingual vascular area on the posterior lateral border of the tongue that is a hemangioma.

Distinguishing Characteristics: Hemangiomas will blanch with pressure, allowing the practitioner to differentiate the vascular lesions from hematomas through diascopy.

Significant Microscopic Features: Hemangiomas appear as large blood-filled vascular channels in the underlying connective tissue. Cavernous hemangiomas exhibit large dilated blood vessels, while the capillary hemangioma demonstrates multiple capillary blood vessels. Figure 13.26 shows the histologic component of a cavernous hemangioma with multiple large dilated blood vessels filled with red blood cells.

Dental Implications: The hemangiomas are evaluated, clinically diagnosed, and watched closely. The only foreseeable problem is the formation of a **thrombus** (thrombosis). When the thrombi exhibit calcification (the term **phlebolith** is given to a calcified thrombus), the lesion may need to be surgically removed.

Differential Diagnosis:
1. Malignant tumors such as Kaposi sarcoma—Chapter 22
2. Varicosity—Chapter 13
3. Venous varix—Chapter 13
4. Hematoma—Chapter 13

Treatment and Prognosis: Some hemangiomas will involute; this is especially true for those found in children, and regression usually occurs within the first decade. Most require no treatment. Occasionally, laser treatment and/or sclerosing solution is recommended for troublesome areas. The prognosis is excellent. Monitoring of the area is needed, since some hemangiomas may enlarge, and development of thrombosis is possible.

FIGURE 13.25. Hemangioma.

NAME: Lymphangioma

Vascular malformations such as the lymphangioma occur during embryogenesis and are present at birth. The lesions consist of lymphatic vessels and vary in size and location. Differentiation of vascular malformation and hemangiomas is often difficult clinically when they are subtle. Lymphangiomas are found on the tongue, buccal mucosa, and floor of the mouth, with the tongue being the most common site. Lymphangiomas present as multilocular lesions, often with some transparency observed. The lesions contain red blood cells within the channels and lymph tissue. It is thought that these lesions may actually be a combination of both hemangioma and lymphangioma. These lesions do not involute. Additionally, a thrill (pulsating of the lesion) may be observed in those that have arteriovenous malformations because of the high vascular flow of blood. Lymphangiomas are surgically removed, but recurrence is common. Figure 13.27 demonstrates a lymphangioma with multinodular surface and a variegated color pattern.

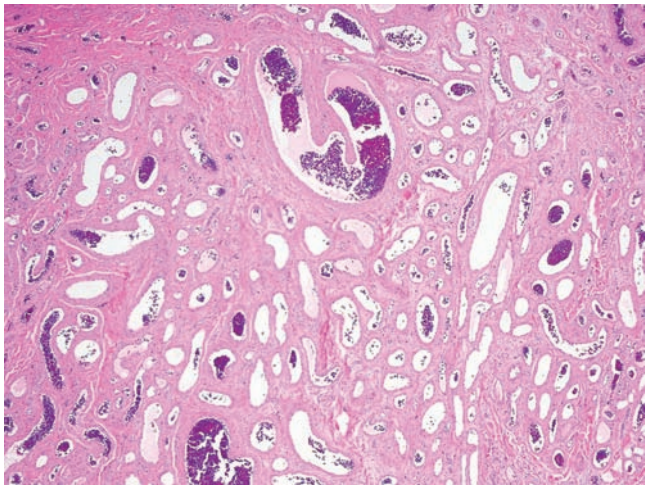

FIGURE 13.26. Histology of a cavernous hemangioma. (Courtesy of Dr. Harvey Kessler.)

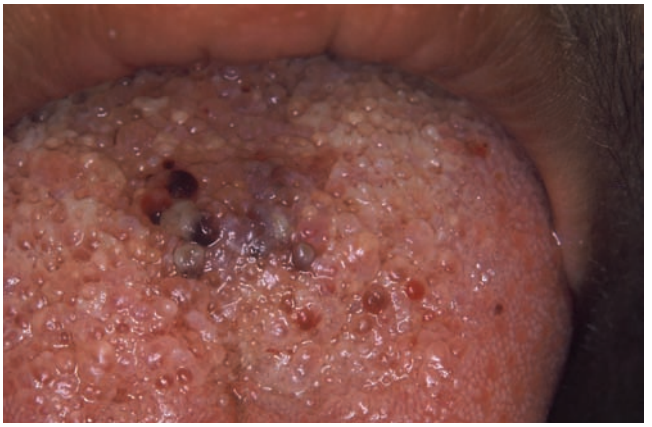

FIGURE 13.27. Lymphangioma. (Courtesy of Dr. Peter Jacobsen.)

NAME: Hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber disease)

Etiology: Hereditary hemorrhagic telangiectasia is an autosomal dominant condition. In the usual sense, telangiectasias are dilated blood vessels that appear as what are commonly known as "spider veins." The blood vessels are small collections of dilated capillaries. These are more of a cosmetic problem for most people, but depending upon the severity of the condition, individuals may be affected to differing degrees.

Method of Transmission: This condition is not contagious.

Epidemiology: There is an equal predilection for males and females. The disease has, as a feature, abnormal dilations of vessels.

Pathogenesis: The oral cavity and external surfaces are affected, and the bright red lesions may bleed profusely. Evidence is usually present at birth and tends to increase throughout life, with special prevalence in adolescence. Thus, diagnosis of the disease may occur at any time. Gastrointestinal bleeding may also be a problem. Another disease that exhibits telangiectasia is known as

scleroderma (see Chapter 23). The person with scleroderma exhibits certain characteristics that are part of the **CREST syndrome.** One of the similarities to hereditary hemorrhagic telangiectasia is the hemorrhagic lesions that occur in both diseases. The two need to be differentiated. CREST syndrome is a systemic sclerosis disease that exhibits not only telangiectasias but also Raynaud phenomenon, esophageal dysfunction, sclerodactyly (the skin becomes stiff and smooth), and formation of cutaneous nodules. Scleroderma and the CREST syndrome are discussed fully in Chapter 23.

Extraoral Characteristics: The skin lesions can appear on the palms, fingers, nail beds, face, and neck. Nasal areas are affected, and the patient may have severe nosebleeds. The skin lesions have a "spider vein" appearance, with fine red-to-pink lines (see Chapter 23).

Perioral and Intraoral Characteristics: The lesions, usually bright red and occurring on the lips and anterior tongue, can rupture, hemorrhage, and appear as an ulcer when traumatized. The papules are about 1 to 2 mm in size and will usually blanch. Figure 13.28 shows oral hereditary hemorrhagic telangiectasia on the dorsum of the tongue and lips. The lips, tongue, and gingival areas are most often affected. The lesions can appear obvious or subtle in some instances, such as those found on the lips of the patient in Figure 13.29.

FIGURE 13.28. Telangiectasia. (Courtesy of Dr. Peter Jacobsen.)

FIGURE 13.29. Telangiectasia. (Langlais RP, Miller CS. Color atlas of common oral diseases. Philadelphia: Lee & Febiger, 1992, with permission.)

Distinguishing Characteristics: Patients who have hereditary hemorrhagic telangiectasia are suspected of the disease because of frequent epistaxis (nose bleeds). The spider veins are another distinguishing characteristic. Bright red hemorrhagic spots are seen in more extreme cases.

Significant Microscopic Features: Microscopic features are dilated, thin-walled vascular spaces that contain erythrocytes.

Dental Implications: The lesions tend to bleed profusely when traumatized, causing a problem with dental treatment for these patients. Depending upon the severity of the disease and the extent of the vascular malformations, a much more serious disease problem may exist, with malformations involving not only the capillaries but also the venous, arterial, and lymphatic channels. There is a concern for brain abscesses and generalized infections. The patient may be premedicated for certain dental procedures depending upon the severity and extent of the procedure.

Differential Diagnosis:

1. Congenital hemangiomas—Chapter 13
2. Congenital vascular malformations—Chapter 13
3. CREST syndrome (scleroderma)—Chapter 23

Prognosis and Treatment: The prognosis is guarded, depending upon the severity. The patient must be monitored throughout life in the severe forms. Anemia may result from blood loss, and there may be complications of the liver and spleen. Preventing hemorrhage is a key factor. This may be problematic in routine dental treatment such as scaling procedures, and precautions are needed, since any disruption of the tissues will cause bleeding. The extent of the bleeding depends upon the severity of the disease.

SUMMARY

- Pyogenic granulomas are benign, inflammatory lesions that are exuberant tissue responses to trauma or local irritation. Other well-known names for these lesions include pregnancy granuloma, pregnancy tumor, or epulis gravidarum.
- The peripheral giant cell granuloma (PGCG) is a reparative and reactive type of tissue response. The lesion also has been called a giant cell epulis. PGCGs are reactive hyperplasia responses to tissue injury, producing an exuberance of tissue in the area of injury.
- Petechiae, ecchymoses, and purpura are hemorrhages in the soft tissue due to either trauma or blood dyscrasias.
- Lichen planus is classified as a cell-mediated immune response producing lesions in various forms that differ in appearance with both red and white lesions. Lichen planus may be a chronic disease with periods of remission. There is an increased risk of oral squamous cell carcinoma (SCC) and esophageal and vaginal cancer.
- All of the disorders in Chapter 13 can have varying appearances, but for the most part, they all fall into the red, blue, or purple range of color.
- Depending upon the depth of a vascular lesion, the color variation is from pink to dark purple in hue.
- Hypersensitivity reactions may be caused by any source in the environment; examples are food products, dental products, environmental factors, and medications.
- Hypersensitivity reactions appear to be delayed cell-mediated immune responses. The cell-mediated immune response is not the classic type I response that is associated with angioedema. Several varieties of contact allergies are known to occur that affect the oral tissues and are considered orofacial disorders.
- Candidiasis is a fungal infection caused by a species of the genus *Candida*. *C. albicans* is the principal species associated with the oral infection.
- The terms *neoplasm* and *tumor* are used interchangeably and are classified as either malignant or benign.
- Erythroplakia refers to a red patch on oral mucous membranes. Erythroplakia encompasses several variations of both velvety red lesions and sometimes those containing a mixture of both red and white lesions, referred to as speckled leukoplakia.
- The varicosity, or varix, is an abnormally dilated and tortuous vein that is an acquired vascular malformation.
- The congenital hemangioma is a developmental anomaly of blood vessels found in infancy and childhood. It consists of benign neoplasms composed of capillaries and venules. The two types of hemangiomas are capillary and cavernous.
- Hereditary hemorrhagic telangiectasia is also known as Rendu-Osler-Weber disease and is an autosomal dominant condition. Multiple hemorrhagic lesions are usually observed.

CHAPTER REVIEW

Case Study 13.1

Your next patient is a 34-year-old pregnant female. This patient is almost 5 months pregnant, reports no complications during the pregnancy, takes no medications, and has scheduled an appointment for a routine cleaning on the advice of her obstetrician. She has no complaints but tells you that she does not floss (see Fig. 13.30).

After examining her intraorally, your findings are the following:

1. The patient has fair oral hygiene, with minimum pocket depth in a 3- to 4-mm range.
2. The patient has 32 teeth.
3. She has multiple crowns and amalgam restorations.
4. The tissue appears normal except for the left hard palate near the rugae. You do notice some small areas of discoloration in multiple areas of the soft palate that are not very noticeable on first glance.

FIGURE 13.30. Courtesy of Dr. Doron Aframain.

Given these findings, please answer the following questions:

1. The patient obviously has an area of concern in the left palate region. How would you describe the red/pink areas?
2. How would you describe the color and texture of the spots? Is the small area of concern red? Would you classify the spots as pedunculated or sessile? What do you think has caused this discoloration? Is this serious, and would you be concerned? What questions would you ask the patient?

FIGURE 13.31. Courtesy of Dr. Doron Aframain.

When you start asking the patient about the spots on the palate, she states that she has another concern and shows you a lesion on her stomach (Fig. 13.31). When you ask how long the spot has been there, she tells you that she always remembers having the small red area on her stomach. She comments that the dentist who placed her crowns commented on the palate lesion.

3. What do you observe in Figure 13.31? How would you describe the red spot on the stomach?
4. What questions do you have for this patient now?
5. What events could have caused the red areas? Do you think that they are connected in source? Or, are they two separate issues?

For answers and additional review activities, log in to **thePoint.lww.com**

Case Study 13.2

A 16-year-old female who is new to your practice is in your office today for an exam and prophy. As you begin speaking with the patient, you notice the growth on her upper lip (Fig. 13.32). She says that she is unhappy with the appearance and states that she is worried that the nodule has developed into a malignancy. The patient gives you the following information:

FIGURE 13.32. Courtesy of Drs. E.S. Goncalesl, Dr. JH Damante, CM Fischer Rubira & LADA Taveira.

- The nodule has been present for 2 years.
- The nodule has been growing slowly.
- It is asymptomatic.
- The nodule bleeds easily.
- The patient used paint thinner on the lesion to stop it from bleeding.
- She has no other complaints and states that her medical history is negative.

Your own clinical review of the lip nodule provides the following:

- The nodule is firm, circumscribed, and somewhat crusted from previous bleeding.
- The nodule is approximately 1 cm in diameter.
- The nodule involves the border of the lip.
- The nodule has a brownish to red-yellow color and shows some ulceration.

1. What disease states would you consider as part of a differential diagnosis?
2. What questions would you ask the patient?

For answers and additional review activities, log in to **thePoint.lww.com**

Critical Thinking Activity

What factors would you review with a patient if you suspected that person might have a lichenoid reaction? What factors might indicate that the person might have a reaction to a medication as opposed to a dental restoration reaction? What characteristics would you search for in your evaluation?
Points to Consider:

1. A person who is having a lichenoid reaction to a medication that is being taken systemically, such as one for hypertension, usually has lichen planus unilaterally.
2. A lichenoid reaction is usually in contact with the offending product, such as an amalgam restoration or crown. If the restoration is removed, the lesion will recede as well if this is the cause of the lesions. A lichenoid reaction is most often unilateral when caused by a specific dental material such as a cement, amalgam, or gold.
3. Remember, some patients have multiple disease states at any given time.

Be sure to consider all possible factors including diet and any other products that are used such as dental toothpaste and mouth rinses. Investigative questioning of the patient usually leads the clinician along the correct path.

Portfolio Possibilities

- Construct a list of medications that are known to cause a lichenoid reaction to use as a reference in your practice.
- Develop a "help" sheet with dental products that do not contain additives or promote allergic responses for patients. The material can be used for patient educational purposes when needed. Refer to Clinical Protocol #6.
- Construct a patient education sheet for your patients who have a problem with certain food products that contain preservatives and coloring additives. This will help the patient avoid future use of these products.

Media Menu

Web Sites

Academy of Nutrition and Dietetics—Information on Health and Nutrition
http://www.eatright.org

American Academy of Oral Medicine
http://www.aaom.com/

American Academy of Family Physicians: Lichen Planus
http://familydoctor.org/familydoctor/en/diseases-conditions/lichen-planus.html

American Lung Association
http://www.lungusa.org

Study Tools

Take advantage of additional online resources to help you study and ace your exams!

- Answers to case studies in the book
- Additional case studies and answers
- Interactive quiz bank with answer feedback
- Fully searchable e-book for quick lookup and studying on-the-go
- Expanded Media Menu with direct links to related Web sites and multimedia resources
- Supplemental references

thePoint Online resources and links are available at http://thepoint.lww.com/DeLong2e

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NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Pyogenic Granuloma	Trauma or irritation Usually during pregnancy and second decade of life	No pus-producing organisms Chronic trauma or irritation	Bright red inflammatory appearance of bulbous tissue Range from a few millimeters to several centimeters	Not true granuloma Hyperplastic granulation tissue	Excision Pregnancy pyogenic granulomas may shrink or disappear after pregnancy.	Scale to remove irritant and promote excellent home care. Rinses such as chlorhexidine (topical antiseptic) may be used.
Peripheral Giant Cell Granuloma	Trauma or irritation to the area Usually in the fifth or sixth decade of life	Response of tissue to injury Hyperplastic tissue response	Growth of tissue. Less vascular than the pyogenic granuloma	Presence of giant cells and capillaries Can be distinguished from the pyogenic by biopsy	Excision and follow up	A biopsy should be taken to rule out more serious conditions. Any chronic growth needs to be diagnosed microscopically.
Petechiae, Ecchymoses, and Purpura	Trauma and blood disorders Hemophilia and leukemia	Blood is collected under the tissue and pooled in the area.	Petechiae—pin point size Purpura—over 2mm Ecchymoses—much larger area covering over 2 cm	NA	Etiology of the petechiae, ecchymoses and purpura must be determined, and more serious etiologies must be ruled out. Treatment depends on the cause of the lesions; certain disease states may require special precautions during treatment.	Identification of medical conditions such as blood diseases and dyscrasias is crucial in obtaining early treatment for the patient.
Lichen Planus	Unknown	Cell-mediated immune response	May present in various forms such as erosive, plaque-like, atrophic, reticular, bullous, and papular	Infiltration of lymphocytes and liquefaction of the basal cell layer Civatte bodies and necrotic keratinocytes	Some forms require no treatment, while others need corticosteroids long-term. When symptoms of vulvo-vaginal-gingival syndrome are present, refer to gynecologist for evaluation of vaginal tissues. Periodic biopsy is needed in most cases when changes occur.	A correct recognition/diagnosis is crucial. Assisting the patient in identifying trigger mechanisms is needed. Avoidance of any harsh dental products and gentle, frequent scaling and prophy is necessary.
Hypersensitivity Reactions	Reaction to a dental product, foods, flavoring agents, and environmental components	Type IV hypersensitivity reaction is produced. Plasma cell gingivitis	Fiery red, bulbous tissue often results A velvety red appearance is often found on the gingiva.	Plasma cells, inflammatory cells, and spongiosis	Identification of the offending products or allergen Discontinuing the agent is necessary.	The clinician must rule out other possible diseases such as mucosal disease states, i.e., lupus, benign mucous membrane pemphigoid (BMMP), papillomavirus (PV), squamous cell carcinoma (SCC).
Candidosis (Candidiasis)	Fungal infection caused by *C. albicans*	Candida is an opportunistic infection and normally resides in the body. When defenses are lowered, the organism becomes more widespread.	May affect the commissures of the mouth causing perlèche May be in several forms such as erythematous, pseudomembranous, chronic hyperplastic, acute, and atrophic	Hyphae are seen in the tissue specimen.	Antifungal medications such as nystatin, clotrimazole oral and vaginal troches. Patients who use corticosteroids may have bouts of Candida and the clinician may need to balance the use of the medications with treating the Candida.	Reinfection by contaminated toothbrushes and by partners prone to the infection may be an issue for some patients. The patient should discard any home care instruments that may be contaminated. Dentures need to be cleaned and decontaminated.
Erythroplakia (Erythroplasia)	Tobacco, alcohol, dietary deficiencies, and lifestyle factors	Epithelial cells no longer produce keratin and undergo cellular changes toward malignancy.	Velvety red or dark pink color Surface may be smooth or pebbly. The surface may have multiple appearances.	Considered premalignant and the earliest form of cancer Increased vascularity	These lesions should be assessed for cancer cells through biopsy. Any surface adjunct device that detects any abnormality warrants a biopsy.	Any red area of tissue that has been present for more than two weeks should be biopsied.
Varicosities	Abnormally dilated and tortuous vein that is an acquired vascular malformation	Arise from a weakness in the vessel wall Most often in older adults	Appear dark blue in most cases and blanch with diascopy	Not applicable—vein and blood supply	Formation of a thrombus is of concern and warrants surgical removal.	Diagnosis of the colored entity is important in ruling out melanoma or serious lesions. Diascopy assists in differentiating vascular and nonvascular lesions.
Hemangioma	Proliferation of blood vessels	Congenital or related to trauma	Intraoral appearance is raised, dark blue and may be single or multiple.	Cavernous appear as large blood-filled vascular channels in the underlying connective tissue. Capillary hemangiomas appear as multiple capillary blood vessels.	Thrombus is of concern or phlebolith when the thrombus exhibits calcification. The lesion would then need to be surgically removed.	Some hemangiomas will involute and this is especially true in children. Monitoring the hemangiomas is important.
Hemorrhagic Telangiectasia	Autosomal dominant Dilated blood vessels	Blood vessels and capillaries bleed easily.	Appear as small, bright red petechiae-like and occur on the lips and tongue	Microscopically resemble dilated, thin-walled vascular spaces that contain erythrocytes	Bleed profusely when injured	Because of the bleeding issues, careful dental procedures that produce as little trauma as possible are necessary. Brain abscesses and generalized infection are possible.

CHAPTER 14

White Lesions

KEY TERMS

Ablated (ablation)
Acanthosis
Atopic/atopy
Callus
Coagulation necrosis
Depapillated
Dysplasia (epithelial)
Erythroleukoplakia
Genokeratosis
Hyperkeratosis
Hyphae
Koebner phenomenon
Leukoplakia
Nuclear hyperchromatism
Premalignant lesion
Proliferative verrucous leukoplakia
Pruritic
Pseudomembrane
Retromolar trigone
Reverse smoking
Speckled leukoplakia
Vacuolated
Verrucous leukoplakia
Vesiculobullous
Wickham stria

LEARNING OUTCOMES

1. Define and use the key terms listed in this chapter.
2. Identify the etiology, method of transmission, and pathogenesis of the white lesions found in the oral cavity.
3. Describe the clinical features of the white lesions discussed in this chapter.
4. Discuss the cellular changes associated with chemical and physical reactions that result in white lesions.
5. List the clinical types of oral lichen planus.
6. Name the most common genokeratosis affecting oral mucosa.
7. Discuss the concept of oral premalignancy at both the cellular and clinical level.
8. Define epithelial dysplasia and note its characteristic cellular features.
9. List the two clinical features that increase the likelihood of a leukoplakia being dysplastic or an invasive carcinoma on biopsy.
10. List clinical changes in an otherwise homogeneous leukoplakia that would redefine it as nonhomogenous.
11. Provide a rationale for performing a biopsy on a leukoplakia.
12. Describe the dental implications of the white lesions discussed in this chapter.

CHAPTER OUTLINE

Variations of Normal
- Fordyce granules
- Leukoedema

Traumatic and Inflammatory Lesions
- Geographic tongue
- Frictional keratosis
- Linea alba
- Cheek chewing
- Nicotine stomatitis
- Hairy tongue
- Chemical and thermal burns

Infections
- Acute pseudomembranous candidiasis
- Chronic hyperplastic candidiasis
- Hairy leukoplakia
- Parulis

Immune System Disorders
- Lichen planus

Genetic or Congenital Disorders
- White sponge nevus

Premalignant/Malignant Disorders
- Leukoplakia
- Oral submucous fibrosis

RELATED CLINICAL PROTOCOLS

#1 Performing a Cytology Smear
#4 Treating Patients with Xerostomia
#5 Diagnosing and Treating Patients with *Candida*
#10 Patient Education: UVA/UVB Skin Protection
#11 Patient Education: Oral Cancer Self-Examination
#13 Alleviating the Oral Symptoms of Mucositis
#19 Oral Health Care Management for the Patient with Cancer
#24 Tobacco Cessation
#25 How to Utilize Nutrition Counseling in Practice

Diseases of the oral mucosa commonly manifest as white lesions, which is a change that is easily detected clinically. White lesions can be the result of **hyperkeratosis** (a thickening of the horny layer of the epidermis or mucosa by increased keratin production), necrosis of epithelial cells (usually caused by an injury), or ischemia (a defective blood supply to the tissues), which undermines the epithelium and results in whiteness. Any condition capable of stimulating keratin production can create a white lesion, since keratin (produced on the surface of the mucosa) turns white when hydrated by saliva.

Some white lesions are entirely innocuous and pose no health risk to patients, while others may be life threatening. The term **leukoplakia** (white patch) is often used to describe an undiagnosed white lesion. This term implies a premalignancy, meaning that untreated leukoplakia has the potential to progress to oral cancer. One should only use this term after formulating a differential diagnosis and ruling out other diseases that can manifest as white plaques. The conditions that mimic leukoplakia are discussed first, while leukoplakia is discussed fully later in the chapter.

Variations of Normal

Some of the white lesions that are encountered within the oral cavity are variations of normal structures or tissues. These need to be recognized by the clinician to differentiate them from pathologic findings.

NAME: Fordyce granules

Etiology: Fordyce granules are normal sebaceous glands that are found in the oral mucosa. Sebaceous glands are also found in hair follicles of the skin, where they secrete an oily substance. Fordyce granules are a feature of normal development.

Method of Transmission: Not applicable

Epidemiology: Fordyce granules affect most of the adult population, as many as 80% in some studies. They are rarely found in children because sebaceous glands develop fully only under the influence of androgenic hormones produced at puberty. Males and females are affected equally (Regezi et al., 2003).

Pathogenesis: Not applicable

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: Fordyce granules appear as superficial yellowish-to-yellowish white, slightly elevated papules (Fig. 14.1).

Fordyce granules are found most commonly on the buccal mucosa and are often bilaterally symmetrical. Patients may have a few to hundreds of Fordyce granules. Patients with these normal structures are asymptomatic.

Distinguishing Characteristics: Fordyce granules are very distinctive in their clinical presentation. Once the clinician

FIGURE 14.1. Fordyce granules. This characteristic presentation of Fordyce granules shows yellowish papules on the buccal mucosa.

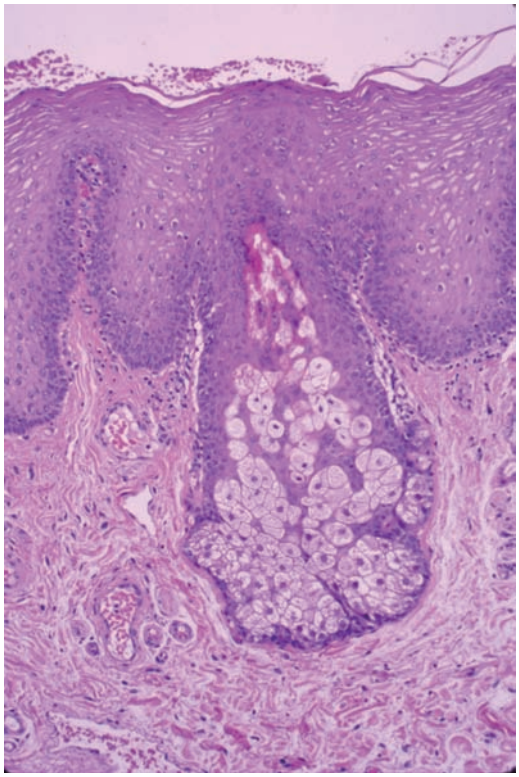

FIGURE 14.2. Fordyce granules. Histology image showing a normal sebaceous gland.

has observed them in several patients, he or she is not likely to mistake them for anything else.

Significant Microscopic Features: Fordyce granules are normal sebaceous glands composed of lobules of rounded cells with abundant cleared, but coarsely granular, cytoplasm (Fig. 14.2).

Dental Implications: None

Differential Diagnosis: None

Treatment and Prognosis: Fordyce granules are normal anatomic findings that require no treatment. Assisting the patient in learning to assess his or her own mouth is a valuable tool. At the same time, it allows the practitioner the opportunity to address a variation of normal as well (see Clinical Protocol #11).

NAME: Leukoedema

Etiology: Leukoedema is sufficiently common that most authorities consider it a variation of normal rather than a pathologic condition.

Method of Transmission: Not applicable

Epidemiology: Leukoedema shows a remarkable racial predilection for blacks and other darker-skinned individuals, but it also occurs in whites (Regezi et al., 2003). It affects males and females equally.

FIGURE 14.3. Leukoedema. Opaque whiteness of the buccal mucosa that disappears when the tissue is stretched is characteristic of leukoedema.

Pathogenesis: Leukoedema is a common mucosal anomaly characterized by intracellular edema and tissue whiteness.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: Leukoedema produces a whitish opaqueness, sometimes with fine wrinkles, of the mucosa (Fig. 14.3). Leukoedema is invariably found on the buccal mucosa and is often bilaterally symmetrical, a feature suggesting a developmental origin. It does not rub off and characteristically disappears when the mucosa is stretched. Normally, the condition can be diagnosed by its characteristic clinical features.

Distinguishing Characteristics: Leukoedema manifests as thin whitish plaques on the buccal mucosa that will dissipate when the tissue is stretched.

Significant Microscopic Features: The epithelium is thickened, and cells are **vacuolated** (having clear spaces within the cell) because of intracellular edema.

Dental Implications: None

Differential Diagnosis: The clinical features and racial predilection are distinctive and there is usually no need for a differential diagnosis.

Treatment and Prognosis: No treatment is indicated. The health care practitioner can teach the patients about the oral cancer self-exam and point out any variation of normal such as leukoedema (see Clinical Protocol #11).

Traumatic and Inflammatory Lesions

Oral white lesions are commonly associated with a traumatic or inflammatory process. Some have an unknown etiology, such as benign migratory glossitis, while others have a known cause, such as mechanical or chemical injury.

NAME: Geographic tongue (GT) (benign migratory glossitis, erythema migrans)

Etiology: Unknown

Method of Transmission: Not applicable

Epidemiology: GT is a relatively common mucosal disorder affecting as many as 2 to 3% of the population according to some studies. Rarely seen in children, GT is typically diagnosed in early to midadulthood. Females are affected about twice as often as males (Kelsch, 2005). Many patients are **atopic** (highly allergic), but to date, there is no evidence that GT represents a hypersensitivity reaction.

Pathogenesis: GT is an inflammatory condition, which is why it is included in this section; however, the cause of the inflammation is unknown.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: The clinical lesions of GT are characteristic and appear as **depapillated** areas (areas of atrophy with loss of filiform papillae). They are usually located on the dorsal surface of the tongue and are either erythematous or pink, surrounded by yellowish white lines that form the margins of the lesions (Fig. 14.4). Typically, lesions will heal, only to reappear at other tongue sites, which give the illusion that the lesions are "migrating." Occasionally, the lesions remain stable. In addition, lesions may affect the ventral surface of the tongue. In rare instances, mucosal sites other than the tongue are affected (erythema migrans). Patients can be asymptomatic or complain of burning or sensitivity. GT is more common in patients who have psoriasis, but it is probably not an element of that condition. It may also be a component of a rare condition called Reiter syndrome, which consists of GT, urethritis, arthritis, and conjunctivitis.

Distinguishing Characteristics: Atrophic and often reddened patches with characteristic yellow-white borders on the dorsal and lateral tongue surfaces are characteristic of this condition.

FIGURE 14.4. Geographic tongue (GT) (benign migratory glossitis). White borders surround a central depapillated area in this classic presentation of GT.

Significant Microscopic Features: The clinical features of GT are usually sufficiently characteristic that a biopsy is not needed to establish the diagnosis. However, a biopsy does show inflammation of the connective tissue with neutrophils migrating through the epithelium, forming small microabscesses.

Dental Implications: GT can be confused with other pathologic conditions. Patients may be alarmed by the appearance of GT when they first notice the condition.

Differential Diagnosis: Considerations include:

1. Candidiasis–Chapters 13 and 14
2. Lichen planus–Chapters 13 and 14
3. Reiter syndrome–Chapter 12
4. Anemia–Chapter 9

Treatment and Prognosis: GT is not a premalignant condition. Asymptomatic patients do not require treatment; symptomatic patients are generally treated with topical corticosteroids to alleviate symptoms.

NAME: Frictional keratosis

Etiology: Physical irritation of the oral mucosa may produce whitish plaques known as frictional keratosis. Historically, white plaques that resulted from physical injury were considered leukoplakia and thought to be premalignant lesions (see the discussion on leukoplakia below in this chapter). However, there has never been convincing evidence that physical injury predisposes to oral malignancy, and accordingly, it is no longer appropriate to designate these lesions as leukoplakia. A white plaque that appears to be the result of physical irritation should currently be called frictional keratosis.

Method of Transmission: Not applicable

Epidemiology: Frictional keratosis is very common; however, there are no data on its prevalence.

Pathogenesis: The oral mucosa has a limited ability to respond to pathologic stimuli. One of its basic adaptive responses is to produce keratin as a protective mechanism against physical injury. This is analogous to a **callus** (overproduction of keratin in the skin as a result of friction) of the skin.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: Frictional keratosis presents as a variably sized, whitish plaque that does not rub off (Fig. 14.5). Keratinization is a feature of chronicity, and an irritant can often be discerned on close clinical inspection.

Distinguishing Characteristics: Frictional keratosis is a white plaque that does not rub off and usually has a cause-and-effect relationship with an irritant.

Significant Microscopic Features: None

Dental Implications: The cause of these lesions should be identified and eliminated. Factitious (self-inflicted)

FIGURE 14.5. Frictional keratosis. This keratotic lesion is secondary to a fractured lingual cusp of a mandibular molar.

FIGURE 14.6. Linea alba. Note the linear elevated keratinized ridge of buccal mucosa.

injuries are sometimes associated with psychiatric disorders. Lesions that do not resolve may be confused with other pathologic conditions, especially leukoplakia.

Differential Diagnosis: Considerations include:

1. Leukoplakia–Chapter 14
2. Lichen planus–Chapters 13 and 14
3. Hyperplastic candidiasis–Chapter 14

Treatment and Prognosis: Because frictional keratosis is an adaptive response, the hyperkeratosis will resolve once the irritant is identified and removed. Clinical resolution confirms the presumptive clinical diagnosis.

NAME: Linea alba

Etiology: Linea alba is a localized form of frictional keratosis due to irritation of the cheek during function. This may indicate bruxism or clenching.

Method of Transmission: Not applicable

Epidemiology: Not applicable

Pathogenesis: Similar to frictional keratosis; linea alba is a reaction to irritation.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: Linea alba is a linear white line along the occlusal plane of the buccal mucosa (Fig. 14.6). Lesions are often bilateral, variably raised, and occasionally scalloped, corresponding to the embrasures between the teeth. Rarely, similar linear keratoses are seen on the lateral surfaces of the tongue.

Distinguishing Characteristics: The appearance of a linear white ridge on the buccal mucosa is characteristic of this condition.

Significant Microscopic Features: None

Dental Implications: None

Differential Diagnosis: None

Treatment and Prognosis: No treatment is indicated. Linea alba is not considered premalignant.

NAME: Cheek chewing (morsicatio buccarum, morsicatio labiorum)

Etiology: Physical irritation (frictional keratosis) causes the lesions associated with cheek or lip chewing.

Method of Transmission: Not applicable

Epidemiology: Not applicable

Pathogenesis: Lesions are associated with overproduction of keratin and damage to the epithelium as a reaction to physical injury.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: Chronic cheek chewing induces hyperkeratosis and continued chewing abrades the tissue, leaving a whitish, irregular surface (Fig. 14.7). Lesions are often bilateral, and acute injury can produce

FIGURE 14.7. Cheek chewing. The macerated, white roughened surface of the buccal mucosa seen in this picture is the result of chronic cheek chewing.

APPLICATION 14.1

Many patients are not aware that they chew their cheeks or may not know of the severity. Very often, the patient will present with heavier areas of trauma during times of stress. Very limited research has been conducted with regard to the effects of **chronic morsicatio buccarum**. However, it is known that pathogens enter the body through any break in the tissue including the mucosa. It is easy to suggest that patients be advised to stop a cheek biting habit, but how does one go about doing it? In many instances, simply showing the patient the areas with a hand mirror or using intraoral photography will provide the awareness needed to assist the patient in decreasing or stopping the chewing.

The following approaches may be helpful in assisting the patient to stop the chewing:

1. Show the patient the area under the dental light. The light provides a clear view of the inside of the mouth for the patient.
2. Depending upon the appearance of the tissue, schedule an oral cancer screening (see Clinical Protocol #12).
3. Discuss whether the patient is under extreme stress at present. Suggest stress reduction techniques or help the patient find someone who may provide the needed guidance.
4. Take intraoral photographs of the area for comparison on future follow-up visits.
5. Determine the use of alcohol and tobacco, which may further place the patient at risk for oral cancer. This is of special concern because of the abraded areas.
6. Develop your own techniques for helping patients break these habits. Once patients are aware that they are chewing on the tissue, they become conscious of their own activity. A rubber band around the wrist or something worn that will remind them throughout the day is usually helpful. Stickers placed on key items that are seen throughout the day work well also. Small circles with "No" and the line through the word work well for some patients.
7. Monitor the abraded areas and be sure to evaluate the areas at a later date and at each subsequent appointment.

areas of redness. Importantly, lesions are confined to the occlusal plane and are not located in the mucobuccal folds where it would be impossible to incur damage due to chewing. Similar lesions can be seen on the labial mucosa or lateral borders of the tongue.

Distinguishing Characteristics: The location of the lesion and the characteristic irregular, white plaques distinguish this condition from other similar lesions.

Significant Microscopic Features: None

Dental Implications: Disruptive oral habits, such as cheek biting, should be discouraged. Long-term inflammation is detrimental to any mucosal tissue.

Differential Diagnosis: These lesions are clinically distinct; however, one might consider white sponge nevus (WSN) (discussed below in this chapter) in a differential diagnosis.

Treatment and Prognosis: The diagnosis can be made from the clinical features and confirmed by a patient history of cheek chewing. The clinical tissue changes are not considered premalignant; therefore, no treatment is indicated. The patient should be educated about the lesion and encouraged to cease the habit (Application 14.1).

NAME: Nicotine stomatitis

Etiology: Heavy smokers often develop keratotic changes of their palatal mucosa. This occurs most frequently in pipe smokers. Heat may play a greater role than irritation from the combustion products of burnt tobacco, as is the case with **reverse smoking** (placing the lit end of the cigarette in the mouth and inhaling).

Method of Transmission: Not applicable

Epidemiology: Not applicable

Pathogenesis: The keratotic changes are a reaction of the palatal mucosa to irritation and heat from smoked tobacco.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: The irritation from smoking produces keratosis of the palatal mucosa and irritation of the minor salivary gland ducts as they exit onto the palate. This in turn produces inflammation and results in small elevations with central erythema (Fig. 14.8). Teeth are often significantly stained.

Distinguishing Characteristics: The whitish palate with small red dots (as shown in Fig. 14.8) combined with a history of smoking is characteristic of this condition.

Significant Microscopic Findings: None

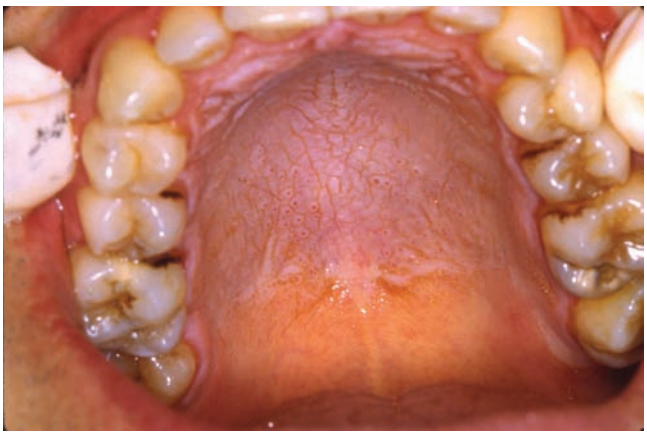

FIGURE 14.8. Nicotine stomatitis. Keratinized palatal mucosa with punctuate inflamed erythematic salivary gland ducts is characteristic of nicotine stomatitis.

Dental Implications: Although the lesion itself is not considered premalignant (except in the case of a lesion associated with reverse smoking), its presence can alert the clinician to the increased risk of development of oral carcinoma in the patient. The clinician can use the presence of the lesion as an educational opportunity to show the patient visible consequences of his or her tobacco habit. The patient should be offered tobacco cessation assistance.

Differential Diagnosis: This clinically distinct lesion does not require consideration of a differential diagnosis.

Treatment and Prognosis: Nicotine stomatitis is diagnosed by its clinical features with confirmation of the patient's smoking habit. Palatal changes will resolve with smoking cessation. The lesion is not considered premalignant, except in the case of reverse smoking. Patients should be encouraged to stop smoking because the habit increases their overall risk of oral and other cancers.

NAME: Hairy tongue

Etiology: The etiology is unknown but there are several risk factors associated with its development, including

- Antibiotics
- Therapeutic radiation therapy
- Smoking
- Oxygenating mouth rinses/peroxide
- Overgrowth of oral flora

Method of Transmission: Not applicable

Epidemiology: Not applicable

Pathogenesis: Hairy tongue represents elongation of the filiform papillae of the dorsal tongue to the extent that the elongated projections look like hair. The reason for the elongation is unknown.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: The hair-like projections can be whitish or, more commonly, brown or black, representing pigments produced by oral flora or exogenous staining due to tobacco smoking (Fig. 14.9). Patients are asymptomatic but often complain of the unsightly appearance. The elongated papillae provide an environment that encourages continued growth of the oral flora, which may result in halitosis. Infection with *Candida albicans* is also an occasional occurrence (see Clinical Protocol #5).

Distinguishing Characteristics: The elongated dorsal tongue papillae and white to brownish-black coloration are characteristic of this condition.

Significant Microscopic Features: None

Differential Diagnosis: None

Treatment and Prognosis: Predisposing factors for this condition should be corrected if possible. Gentle physical debridement with a toothbrush or tongue scraper is helpful. Often, antimicrobial mouth rinses, such as chlorhexidine gluconate, are prescribed. Essential oil mouth rinses may also be recommended. If a candidal infection is present, antifungal therapy should be given.

FIGURE 14.9. Hairy tongue. Note the elongated filiform papillae and discolored surface that are characteristic of this condition.

NAME: Chemical and thermal burns

Etiology: Many chemicals or drugs are caustic and can burn the mucosa if they come in contact with it. Generally, this is caused by a group of chemicals that were not intended for topical placement on oral mucosa. The best example is aspirin burn, which occurs when patients place an aspirin tablet on the mucosa opposite a tooth that hurts. Many burns are produced by patients treating oral pain with numerous over-the-counter (OTC) medications or home remedies. Many different types of acids and alkalis can produce tissue necrosis, as can phenols, silver nitrate, and hydrogen peroxide. A variety of dental medicaments have also been implicated in mucosal chemical burns. Thermal burns can be caused by hot foods or implements placed in the mouth or by electric currents.

Method of Transmission: Not applicable

Epidemiology: Not applicable

Pathogenesis: Chemical and thermal burns often produce necrosis of the epithelium, which turns it white.

Extraoral Characteristics: Burns can occur on the extraoral skin, but these patients are not likely to present to a dental office for evaluation.

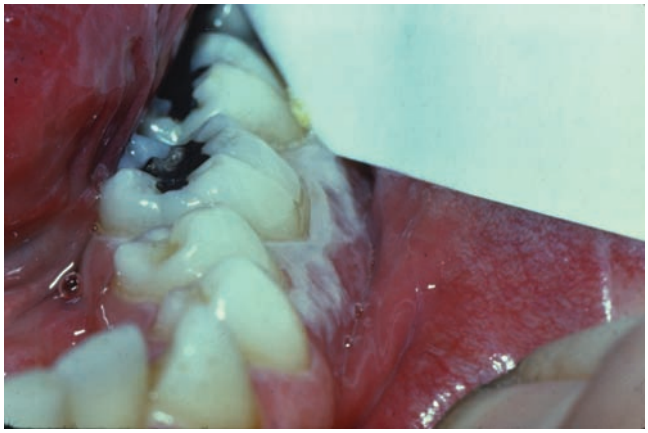

FIGURE 14.10. Chemical burn. This burn occurred when the patient placed an over-the-counter medication containing eugenol on the gingiva to relieve the pain of a toothache.

Perioral and Intraoral Characteristics: Most chemical and thermal burns manifest as white plaques of variable size (Fig. 14.10). Early or mild lesions do not rub off, whereas more severe lesions can often be removed with pressure from a tongue blade, leaving a raw and occasionally bleeding base. The ability to scrape a burn off depends upon the extent of the injury and is not a prerequisite clinical finding for the diagnosis.

Distinguishing Characteristics: Chemical and thermal burns appear as localized white plaques that may or may not be rubbed off. A careful review of the patient's history with follow-up questions may uncover the actual event associated with the burn and thereby provide a definitive diagnosis.

Significant Microscopic Features: Burns produce **coagulation necrosis,** in which the cells become necrotic but maintain their original cellular outline (Fig. 14.11).

Dental Implications: These lesions may occasionally be confused with other pathologic conditions. In addition, the patient should be educated about the proper use of medications such as aspirin.

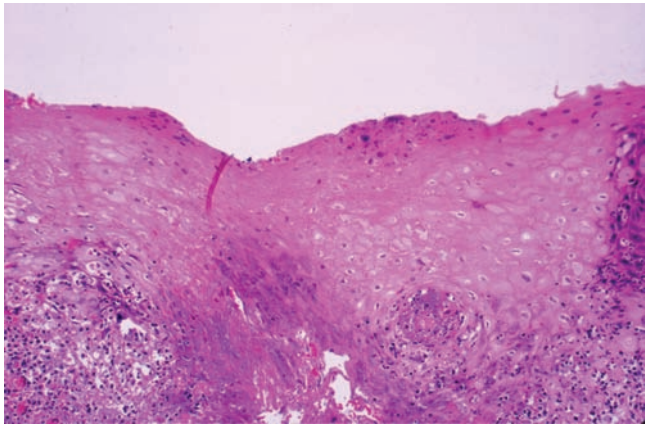

FIGURE 14.11. Coagulation necrosis. This histology slide depicts coagulation necrosis of the surface epithelium from a chemical burn. Note the cells within the epithelium that no longer have nuclei but still maintain their shape.

Differential Diagnosis: The diagnosis of a chemical or thermal burn can be established from the clinical features and identification of the offending chemical or hot substance. Other white lesions should be included in a differential diagnosis, including

- Frictional keratosis–Chapter 14
- Hyperplastic candidiasis–Chapter 14
- Lichen planus–Chapters 13 and 14

Treatment and Prognosis: The lesion will heal once the offending chemical is withdrawn and/or more hot substances do not traumatize the tissue.

Infections

Some white lesions arise from a known source of infection such as candidiasis, a fungal infection. Another example is the parulis, which arises because of an acute infection due to a nonvital tooth or a periodontal pocket. In this section, we discuss infections that manifest as white lesions, two specific forms of candidiasis (acute pseudomembranous candidiasis and chronic hyperplastic candidiasis) hairy leukoplakia (HL), and the parulis.

NAME: Acute pseudomembranous candidiasis (candidosis, moniliasis, thrush)

Etiology: Candidiasis or candidosis is caused by species of *Candida*, usually *albicans*, which is a yeast-like fungus. Most patients harbor yeasts (*Candida* species) as part of their normal oral flora. Candidiasis usually represents an overgrowth of *Candida* that is already present in the mouth. The organism has extremely low virulence and tends not to produce infection in healthy patients. When it does cause disease, a variety of predisposing factors are present that appear to alter the oral environment or systemic status of the host and allow an opportunity for the organism to grow. The following are some of the more common factors that predispose an individual to infection with *C. albicans:*

- Systemic broad-spectrum antibiotic therapy
- Systemic, topical, or aerosolized corticosteroid use
- Smoking
- Xerostomia
- Immune system disorders
- Diabetes

Method of Transmission: While candidiasis is an infection, it is not highly transmissible. Candidiasis is considered an opportunistic infection.

Epidemiology: Candidiasis has a worldwide distribution and is commonly found in immunocompromised patients and the elderly who have other predisposing factors.

Pathogenesis: Acute pseudomembranous candidiasis, also known as thrush, is the most clinically characteristic form

of yeast infection. This is the form of candidiasis commonly encountered in newborns who contract the infection from the birth canal. The infectious organisms either produce necrosis of the surface epithelium, which turns white and rubs off, or they produce erythema resulting from the body's reaction to the organism. The erythematic forms of this infection are discussed in Chapter 13.

Extraoral Characteristics: Candidiasis can occur in any epithelial surface of the body but is especially common in areas that are consistently warm and moist, such as the feet and areas where skin overlaps, for example, in overweight persons where the rolls of skin and fat tissue overlap each other.

Perioral and Intraoral Characteristics: Acute pseudomembranous candidiasis manifests as multiple, raised, whitish, cordlike plaques with variable surrounding erythema (Fig. 14.12). The plaques are always multiple, and it is not unusual for large areas of the oral mucosa to be affected. Because it represents an infection, patients are almost always symptomatic and complain of pain, discomfort, or burning. The plaques can be scrapped off with a tongue blade or stiff instrument, hence the designation **pseudomembranous.** Many experts state that once a plaque is removed, it will reveal an erythematous or bleeding base. Most often, you will see erythema because without the dead plaque covering it, the inflammation in the underlying tissues, representing the body's reaction to the infection, can be seen.

Distinguishing Characteristics: The ability to scrape the pseudomembranes off is a diagnostic feature of this form of candidiasis. However, the dental hygienist almost never sees a "bleeding" base, since it would require scraping the tissues hard enough to remove the entire thickness of epithelium down into the underlying connective tissue.

Significant Microscopic Features: Candidal organisms typically grow on the surface of the mucosa and produce necrosis of superficial keratinocytes. As the cells die, they lie on the surface of the tissue as white plaques matted together by the **hyphae** (elongated form) of the organisms (Fig. 14.13).

FIGURE 14.12. Pseudomembranous candidiasis. Multiple whitish plaques that scrape off leaving an erythematous base are characteristic of this form of candidiasis.

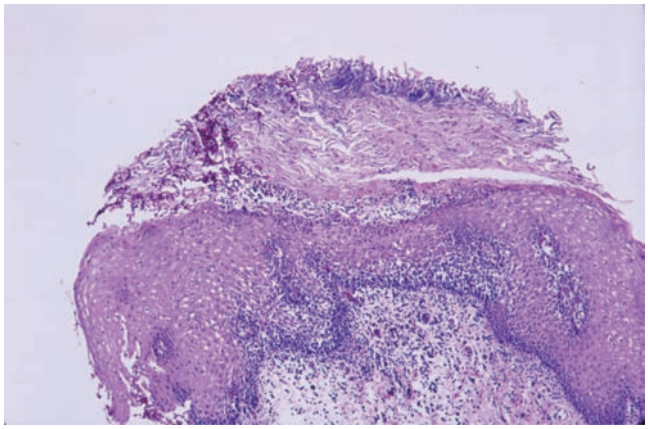

FIGURE 14.13. Pseudomembranous candidiasis. Histology slide of the necrotic surface cells in a pseudomembrane showing *Candida* organisms and a thickened epithelial surface.

Dental Implications: Candidiasis is an infection that needs to be diagnosed and treated. The tendency for this infection to occur in immunocompromised patients should prompt the dental professional to carefully review the patient's medical history for any sign of undiagnosed systemic problems (see Clinical Protocol #5).

Differential Diagnosis: Most white lesions that rub off are candidal infections, burns, or **vesiculobullous** (characterized by fluid filled blisters) diseases in which the epithelium sloughs.

Treatment and Prognosis: Once the diagnosis is established, a variety of effective antifungal medications are used for treatment. Many clinicians treat the infection with topical medications such as nystatin oral suspension or clotrimazole troches. Effective systemic medication is also available, such as fluconazole.

NAME: Chronic hyperplastic candidiasis (candidal leukoplakia)

Etiology: Hyperplastic candidiasis is also caused by a species of *Candida*, usually *albicans*.

Method of Transmission: Chronic hyperplastic candidiasis, like pseudomembranous candidiasis, is not considered to be highly transmissible.

Epidemiology: Chronic hyperplastic candidiasis is a very rare form of yeast infection.

Pathogenesis: There is experimental evidence that *C. albicans* may stimulate a hyperplastic reaction in the mucosal tissues of some individuals. The reason this type of response occurs in some individuals and not in others is not known. In addition, this is the only form of candidiasis that is considered to have a very low malignant transformation potential. Up to 15% of cases may progress into dysplastic lesions, which in turn may progress to cancer (Sitheeque & Samaranayake, 2003). (Refer to the discussion on epithelial dysplasia in the following section on leukoplakia.)

FIGURE 14.14. Chronic hyperplastic candidiasis. A characteristic white plaque that does not rub off is shown on the lateral border of the tongue.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: Chronic hyperplastic candidiasis manifests as a thickened, often raised, whitish plaque that does not rub off. Lesions commonly affect the tongue or commissure (Fig. 14.14). The lesions have no distinctive clinical features and are indistinguishable from leukoplakia. In fact, another term for the condition is candidal leukoplakia.

Distinguishing Characteristics: Hyperplastic candidiasis cannot be clinically distinguished from other white lesions that do not wipe off.

Significant Microscopic Features: The diagnosis can only be established by a biopsy that demonstrates hyperkeratosis, epithelial hyperplasia, and the causative hyphae of the organism in the superficial keratin.

Dental Implications: This lesion is rare, but it is considered premalignant. Chronic forms of candidiasis are also an indication that the person's immune system may be deficient.

Differential Diagnosis: Chronic hyperplastic candidiasis is indistinguishable from leukoplakia.

Treatment and Prognosis: Treatments include systemic antifungals, topical application of vitamin A/retinoids and β-carotenes, laser surgery, and conventional surgical excision. The treatment of these lesions is somewhat controversial, because treatment does not universally result in resolution of the lesion. Furthermore, treatment does not necessarily prevent the development of epithelial dysplasia and progression to cancer (Sitheeque & Samaranayake, 2003). However, it is only this form of candidiasis that shows any malignant potential. The more common forms of erythematous or pseudomembranous candidiasis show no relation to oral cancer.

NAME: Hairy leukoplakia (HL)

Etiology: HL is caused by an infection with Epstein-Barr virus (EBV) secondary to immunosuppression. HL is linked to the immunosuppression that results from infection with the human immunodeficiency virus (HIV). However, HL is well documented in other immunosuppressed patients, as well; for example, those who are taking chemotherapy for malignancy or immunosuppression therapy for organ transplantation.

Method of Transmission: Not applicable

Epidemiology: HL occurs predominantly in HIV-infected patients. The incidence of HL has decreased significantly now that HIV-positive patients are treated with aggressive antiretroviral chemotherapy.

Pathogenesis: Unknown

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: HL produces whitish plaques that do not rub off. They usually affect the lateral borders of the tongue, often bilaterally, where they appear as vertical, raised ridges or sometimes as irregular flattened lesions (Fig. 14.15). Rarely, HL will affect mucosal surfaces other than the tongue. Patients are typically asymptomatic.

Distinguishing Characteristics: HL characteristically presents as white plaques, often with vertical raised ridges, bilaterally on the tongue in immunosuppressed patients.

Significant Microscopic Features: The diagnosis of HL is made by biopsy with demonstration of EBV in the surface epithelium. The name HL comes from the histologic appearance, in which there is hyperkeratosis with exophytic extensions of keratin that appear somewhat like hair. Many of the superficial keratinocytes show cytoplasmic clearing with intranuclear viral inclusions.

Dental Implications: HL is a significant diagnosis because it is a relatively accurate predictor of rapid progression from HIV latent infection to AIDS. (See also HIV/AIDS, Chapter 22.)

Differential Diagnosis: Several of the more keratotic white lesions discussed in this chapter are included in a differential

FIGURE 14.15. Hairy leukoplakia (HL). The characteristic presentation of HL is bilateral white plaques along the lateral border of the tongue. This HL lesion is on the lateral border of the tongue in a human immunodeficiency virus (HIV)-positive male.

diagnosis, including frictional keratosis, lichen planus (LP), candidiasis, and thermal and chemical burns.

Treatment and Prognosis: Antiviral therapy often produces improvement or resolution of the lesion; however, recurrence is not uncommon. There is no evidence that HL has the potential for malignant transformation.

NAME: Parulis

Parulis is a swelling of the gingiva caused by a draining sinus tract from an odontogenic infection of either periodontal or pulpal origin. The swelling is due to purulent exudate (pus), which is more yellowish than white. When pus is encountered clinically, the source of odontogenic infection should be determined and treated.

Immune System Disorders

A variety of skin conditions can also affect mucous membranes. Many of these are autoimmune disorders or immune-mediated inflammatory conditions.

NAME: Lichen planus (LP)

Etiology: LP is a chronic immune-mediated mucocutaneous disorder. T lymphocytes are recruited to the skin or oral mucosa where they produce damage to the surface epithelium.

Method of Transmission: Not applicable

Epidemiology: LP is the most common dermatologic condition that manifests with cutaneous as well as oral lesions. Refer to Chapter 13 for detailed information on the epidemiology of LP.

Pathogenesis: While the reaction suggests that the body is reacting to an antigen within the surface epithelium, to date the specific antigen(s) has not been identified. Some authorities consider LP to be an autoimmune disorder; however, until an antigen is identified, it is premature to consider LP an autoimmune disease.

Extraoral Characteristics: The characteristic skin lesions are purplish, raised papules with a keratotic white surface pattern of very fine interlacing lines called **Wickham striae.** Lesions are also **pruritic** (itchy) and typically affect the legs and forearms.

Perioral and Intraoral Characteristics: LP is another condition that appears in a variety of clinical patterns, including white lesions, red lesions, and ulcers. This section focuses primarily on the white lesions, which are the most distinctive clinically. Other forms of this condition are discussed in Chapter 13 and are also mentioned in Chapter 23 regarding skin lesions. Two forms of LP appear as white lesions: the reticular and plaque-like forms.

The *reticular or striate form* of LP is the most common and is characteristic of the various presentations. It produces a lacy pattern of Wickham striae that do not rub off (Fig. 14.16). The lesions affect the buccal mucosa, usually bilaterally, but may also affect the gingiva. The reticular form of LP tends to be asymptomatic, but some patients will complain of a textural change. One of the most common sites to see LP is in the postbuccal mucosa in the lower mucobuccal fold, which is often traumatized from routine functioning. LP tends to affect sites prone to trauma, an occurrence known as the **Koebner phenomenon** (ability of a disease to affect chronically irritated tissue).

FIGURE 14.16. Lichen planus (LP). Note the typical reticular or striate pattern of Wickham striae.

The *plaque* form of LP is less common than the reticular form and manifests as a whitish plaque. This plaque has no clinically distinguishing features and appears similar to leukoplakia.

Distinguishing Characteristics: Wickham striae observed bilaterally on the buccal mucosa and possibly on the gingiva are characteristic of this disorder.

Significant Microscopic Features: The epithelium is hyperkeratotic, with irregular rete ridges that are often angular and described as "saw tooth." There is significant basal epithelial cell damage with liquefaction degeneration and an immune band-like infiltrate of small lymphocytes in the underlying connective tissue.

Dental Implications: LP is often confused with other pathologic processes. Symptomatic patients require diagnosis and treatment. There is controversy regarding the premalignant nature of LP, and case studies as well as editorials are published on both sides of this issue. All agree that the lesions should be carefully monitored.

Differential Diagnosis: Other white lesions may have similar appearances such as:

1. Candidiasis–Chapter 14
2. Leukoplakia–Chapter 14

Treatment and Prognosis: The reticular and plaque forms of LP are generally asymptomatic, and patients usually do not require treatment unless the disease becomes erosive and symptomatic. Biopsy is usually not indicated unless a change occurs after a confirmed diagnosis is made. Erosive lesions are considered more suspicious, since they have been

reported to become squamous cell carcinoma in some cases. However, the malignant potential of LP is controversial, and lesions not responding to traditional treatment, or lesions showing growth or a mass effect, should have a biopsy performed (see Clinical Protocol 3).

Genetic or Congenital Disorders

Genokeratoses represent a variety of inherited oral mucosal disorders that produce keratinized (white) lesions of the oral mucosa. Because these lesions are inherited, they tend to appear at an early age or at birth and are often multifocal, affecting large areas of the oral mucosa. The most common condition of this type is WSN.

NAME: White sponge nevus (WSN)

Etiology: WSN is an inherited condition caused by the mutation of certain keratin genes. WSN is usually apparent in childhood but is sometimes not noticed until adolescence.

Method of Transmission: WSN follows an autosomal dominant inheritance pattern. Occasionally, cases appear in individuals with no family history of the disorder.

Epidemiology: This is a rare condition.

Pathogenesis: The disorder involves an autosomal dominant trait, and a diagnosis is made rapidly when a family history already exists.

Extraoral Characteristics: Rarely, WSN affects the upper aerodigestive tract mucosa and anogenital areas.

Perioral and Intraoral Characteristics: WSN tends to produce widespread keratinization of the buccal mucosa and often the labial mucosa (Fig. 14.17). The lesions do not rub off.

Distinguishing Characteristics: Widespread white plaques on the buccal and labial mucosa that do not rub off are characteristic of this disorder.

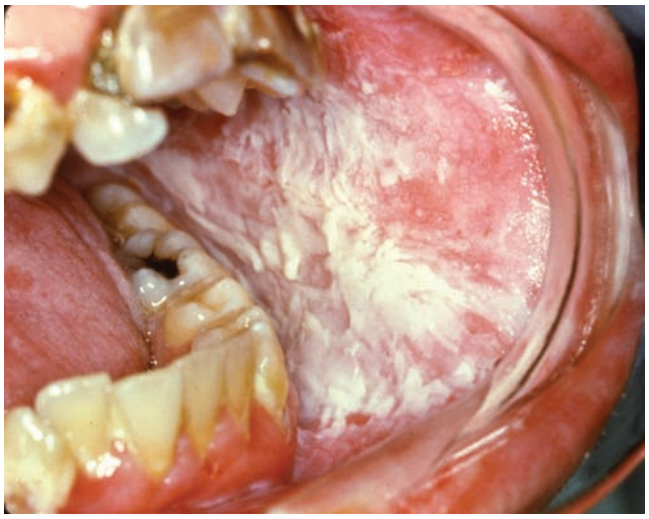

FIGURE 14.17. White sponge nevus (WSN). Observe the extensive keratotic plaques that extend into mucobuccal folds.

Significant Microscopic Features: Hyperkeratosis, **acanthosis** (thickening of the prickle cell layer of the epithelium), and cytoplasmic clearing of the epithelial cells are microscopic findings related to this disorder.

Dental Implications: Occasionally, these lesions present as a cosmetic problem.

Differential Diagnosis: Because of the cheek involvement, the lesions show some similarity to cheek chewing. The lesions of WSN, however, invariably affect mucobuccal folds, sites that are virtually impossible to chew. Other possibilities include leukoedema, leukoplakia, and LP, all discussed in this chapter.

Treatment and Prognosis: Once a diagnosis of WSN is confirmed, no other treatment is needed, and the prognosis is excellent.

Premalignant/Malignant Disorders

A **premalignant** lesion can be defined as a clinically detectable morphologic tissue change that has a higher risk of developing into oral cancer than normal tissue. Oral leukoplakia is the most common form of premalignant lesion found in the oral cavity. A premalignant condition is defined as a generalized state associated with a significantly increased risk of cancer that can develop anywhere within the oral cavity, not just within a preexisting lesion (Reibel, 2003). Oral submucous fibrosis (OSF) and oral LP are examples of premalignant conditions. Oral LP is discussed above; leukoplakia and OSF are discussed below.

NAME: Leukoplakia

Leukoplakia is defined by the World Health Organization as "a white patch or plaque that does not rub off and that cannot be diagnosed clinically or pathologically as any specific disease." Accordingly, leukoplakia is a descriptive clinical term for a white patch with no clinically distinguishing features. It is also a diagnosis by exclusion. The term should only be used after a thorough differential diagnosis has been considered, and all specific conditions producing mucosal whiteness have been ruled out.

Etiology: Historically, chronic irritation was thought to be an etiologic factor in many leukoplakias. However, there has never been sound scientific documentation that physical irritation of tissues leads to malignancy. Therefore, white lesions that are clearly the result of physical irritation should not be diagnosed as leukoplakia but should be called frictional keratoses. The most important etiologic factor associated with leukoplakia is tobacco, both smoked and topical. Approximately 50% of leukoplakias in smokers will resolve with smoking cessation, and over 95% of spit tobacco lesions resolve with cessation (Wright, 2003). Leukoplakias do however occur in nonsmokers.

Method of Transmission: Not applicable

Epidemiology: Leukoplakia has a worldwide distribution and is found most commonly where tobacco use is prevalent and acceptable. It is typically found in less than 1% of nonsmokers but from 6% to as high as 60% of smokers in some studies. Men are more frequently affected, but with the social acceptance of smoking in women, more women are affected today.

Pathogenesis: Leukoplakia arises from genetic mutations to the epithelial cells following exposure to carcinogens (see Chapter 5). Leukoplakia is considered a premalignant lesion (a lesion from which a malignant neoplasm may develop in a significant number of cases). Oral cancer does not arise from normal oral epithelial cells. Rather, as normal cells evolve into cancer, they develop microscopic changes that are known as epithelial dysplasia. Fortunately, dysplastic epithelium tends to produce clinically detectable alteration of the oral mucosa. These lesions tend to be white (leukoplakia) and/or red (erythroplakia). It is well documented that some untreated leukoplakias will progress into squamous cell carcinoma. However, many lesions take years to evolve into cancer, and some may never evolve. The significance of this slow progression is that many patients will have clinically detectable premalignant lesions that may persist for years (see Clinical Protocol 12). Detection and therapeutic intervention at the premalignant stage can potentially prevent the development of oral cancer. There are two clinical features of leukoplakia that can help to identify the dysplastic lesions: (1) the anatomic site involved and (2) whether or not the lesion is homogeneous. The overall likelihood that a leukoplakia will show microscopic evidence of dysplasia or invasive disease is 20%. Leukoplakias involving certain anatomic sites have a greater than 20% likelihood of showing dysplasia or invasion (Cawson et al., 2001). These are known as high-risk sites, and they correspond to sites prone to develop malignancy such as the lower lip, the floor of the mouth, the lateral and ventral tongue, the **retromolar trigone** (the soft tissue area posterior to the mandibular molars toward the pharynx), and the lateral soft palate. The highest risk site is the floor of mouth and ventral tongue, where just over 40% of leukoplakias will show dysplasia/carcinoma. Presence on the lower lip increases the risk to 35% and on the lateral tongue to approximately 25% (Cawson et al., 2001). In addition, nonhomogeneous lesions (lesions containing redness, ulceration, or a verrucous surface architecture) will show evidence of dysplasia/carcinoma at a considerably higher rate (Cawson et al., 2001). Longitudinal studies have shown conclusively that some leukoplakias will progress to carcinoma if untreated, and traditionally this has occurred in approximately 5% of lesions. However, earlier studies did not distinguish between dysplastic and nondysplastic lesions. Newer studies have shown that approximately 1% of nondysplastic leukoplakias and 15% of dysplastic lesions will progress to carcinoma over time if untreated (Cowan et al., 2001).

FIGURE 14.18. Leukoplakia. Shown is a characteristic leukoplakia of left lateral border of the tongue.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: The clinical features of leukoplakia are highly variable, manifesting in a variety of shapes and sizes and affecting virtually any mucosal surface (Fig. 14.18). Lesions range from minute (millimeters) to several centimeters in size. Most lesions are single, but occasionally, multiple lesions are encountered. Most lesions are soft on palpation, but depending on the thickness of the surface keratin, some lesions feel leathery. Palpating a firm mass (induration) under the surface of the leukoplakia is a strong indicator that the lesion may represent invasive squamous cell carcinoma. Patients with leukoplakia are asymptomatic, and a thorough oral examination is the most important means of detection.

Leukoplakias in smokers can affect any site. The most commonly used spit tobacco that produces keratosis is snuff, and these lesions are often referred to as snuff dippers keratosis or snuff dippers pouch (Fig. 14.19). The mucosa is often corrugated, and the adjacent teeth are usually stained and exhibit gingival recession.

FIGURE 14.19. Snuff dippers keratosis. Classic presentation of snuff dippers keratosis at site of snuff placement.

FIGURE 14.20. Actinic keratosis. Note the crusted lip and loss of a distinct vermilion border on this patient.

Leukoplakias of the lower lip are invariably related to chronic sun damage and are termed actinic or solar keratosis (see Chapter 23 on skin lesions) (see Clinical Protocol 10). Sun damage to the lower lip produces atrophy of the vermilion border with loss of the sharp demarcation between the vermilion border and skin. The vermilion is variably white, with or without areas of erosion and/or crusting (Fig. 14.20).

Some authorities subclassify leukoplakia as homogeneous or nonhomogeneous. In some cases, leukoplakias will also have areas of redness, ulceration, or a pebbly or verrucous surface. These later clinical changes make the lesion nonhomogeneous. These lesions have also been described as

1. **Speckled leukoplakia (erythroleukoplakia).** These lesions exhibit both red and white components (Figs. 14.21 and 14.22) (see Chapter 13 for more on red lesions).
2. **Verrucous leukoplakia.** These lesions show an irregular or verrucous surface texture.
3. **Proliferative verrucous leukoplakia.** Proliferative verrucous leukoplakia is a particularly aggressive form of leukoplakia that tends to be multifocal and progressive and normally shows a high incidence of progression to carcinoma (Fig. 14.23). This form of leukoplakia exhibits a tendency to form on the gingival tissues, where it is associated with the greatest potential for malignant transformation (Shopper et al., 2004).

FIGURE 14.21. Speckled leukoplakia. This tongue lesion exhibits discrete red and white areas.

FIGURE 14.22. Speckled leukoplakia. Another example of a speckled leukoplakia or erythroleukoplakia with posterior white (leukoplakia) and anterior red (erythroplakia) portions.

Distinguishing Characteristics: Leukoplakia is not clinically distinguishable from other white lesions that do not rub off.

Significant Microscopic Features: If large numbers of biopsies are performed on leukoplakias, approximately 80% will show hyperkeratosis (thickening of the stratum corneum layer), with or without acanthosis. The remaining 20% will show some grade of dysplasia, carcinoma in situ, or invasive squamous cell carcinoma (Waldron & Shafer, 1975). The most accurate predictor of malignant progression is the presence of epithelial dysplasia. Dysplasia represents the morphologic changes the cells go through as they evolve from normal to malignant, and as such, it represents premalignant change. The presence of dysplasia can only be ascertained microscopically following a biopsy. The cellular features that characterize dysplasia are well recognized and include the following:

FIGURE 14.23. Proliferative verrucous leukoplakia. This white lesion on the alveolar ridge had a verrucous surface texture and was determined to be a proliferative verrucous leukoplakia. (Courtesy of Dr. John Wright.)

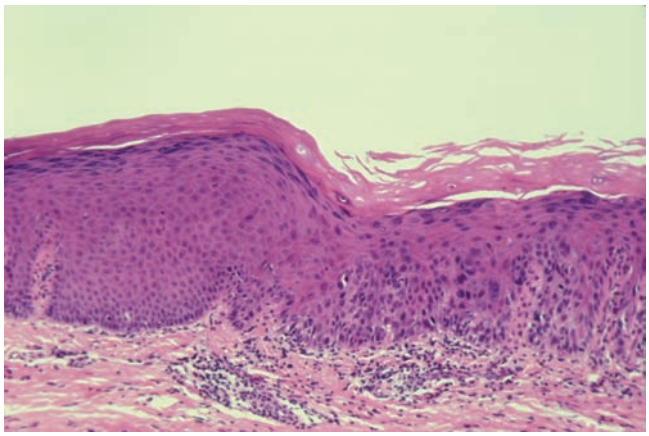

FIGURE 14.24. Mild epithelial dysplasia. Mild epithelial dysplasia on the right displaying minimal cytologic change and alteration of maturation compared with normal epithelium on the left.

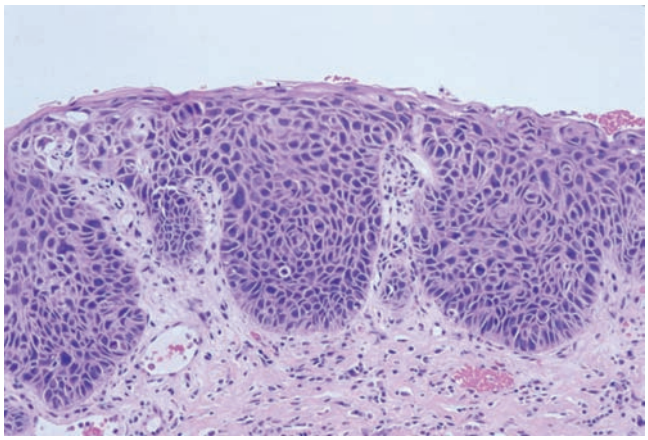

FIGURE 14.26. Severe epithelial dysplasia. Severe epithelial dysplasia displaying significant nuclear hyperchromatism, pleomorphism, and altered maturation affecting most of the epithelium.

- Increase in cellular nuclear/cytoplasmic ratio
- Rounded or irregular rete ridges
- Altered maturation
- Increased mitoses, atypical mitoses, mitoses in upper layers of epithelium
- Pleomorphism (variation in size and shape)
- **Nuclear hyperchromatism** (chromosomal material that stains darkly when exposed to specific staining solutions)
- Enlarged nucleoli
- Loss of cellular cohesion
- Abnormal keratinization patterns

Not all features of dysplasia are present in all lesions; however, those present tend to occur in varying degrees. Accordingly, when assessing dysplasia, most pathologists subjectively grade the dysplasia according to its severity. Dysplasias are graded as mild, moderate, or severe. Figure 14.24 represents mild dysplasia, Figure 14.25 represents moderate dysplasia, and Figure 14.26 depicts severe dysplasia. Carcinoma in situ represents a lesion in which the cells look malignant but are still confined to the epithelium (in situ). Figure 14.27 shows carcinoma in situ, and Figure 14.28 depicts invasive cancer.

Ultimately, these abnormal cells will leave the epithelium and invade deeper structures, and this traditionally is when the process becomes malignant. The cellular features of premalignant and malignant lesions are similar; the main difference is the presence or absence of invasion.

Differential Diagnosis: In no other condition is differential diagnosis more important that in leukoplakia, because leukoplakia is a diagnosis by exclusion. Only after all other

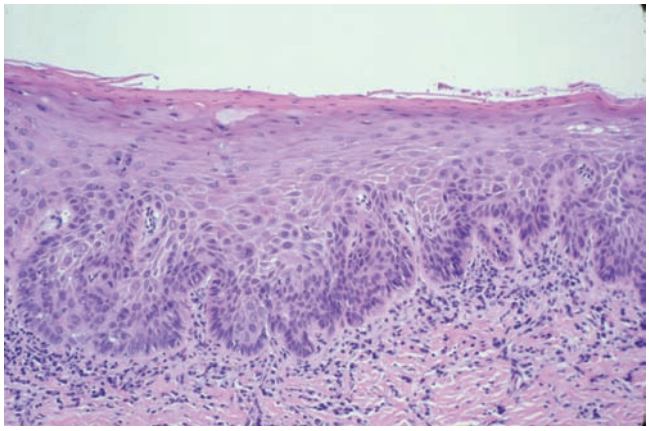

FIGURE 14.25. Moderate epithelial dysplasia. Moderate epithelial dysplasia displaying increasing cytologic atypia and alteration of maturation in the lower half of the epithelium.

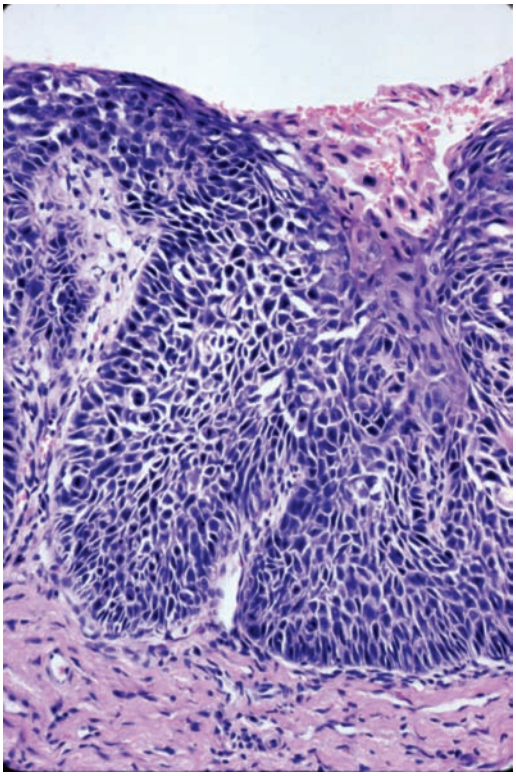

FIGURE 14.27. Carcinoma in situ.

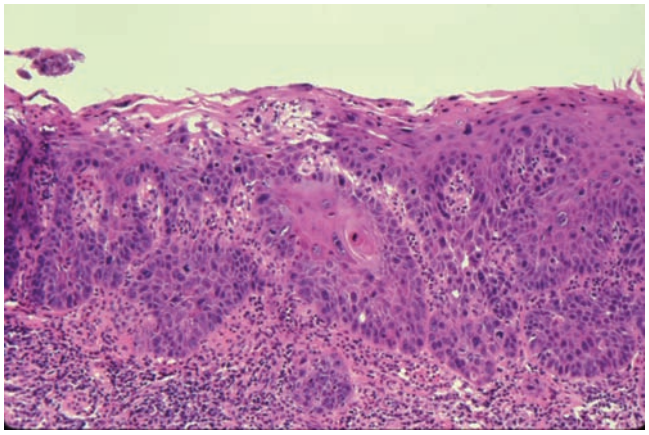

FIGURE 14.28. Superficially invasive squamous cell carcinoma. Note the penetration of the basement membrane by the cancer cells in this histology slide. (Courtesy of Dr. John Wright.)

white lesions are considered and ruled out is leukoplakia the appropriate clinical diagnosis. The speckled form of leukoplakia shows clinical features similar to those of pseudomembranous candidiasis, but unlike candidiasis, the speckled whitish elevations do not rub off.

Treatment and Prognosis: Biopsies should be performed on leukoplakias, since microscopic examination is the only way to accurately assess the presence of epithelial dysplasia. A small number of leukoplakias actually represent early invasive cancer, but one that was discovered before the cells could replicate sufficiently to produce a mass or swelling typically associated with cancer. The odds are in the patient's favor, as most leukoplakias are nondysplastic, but biopsy is mandatory to detect the ones that are dysplastic. Treatment decisions are best made following a biopsy and a determination of microscopic findings. Nondysplastic lesions are best managed by altering or eliminating risk factors such as tobacco use. With tobacco cessation, approximately 50% of leukoplakias associated with smoked tobacco and over 95% of those with spit tobacco regress (Cowan et al., 2001). Dysplastic lesions are ideally managed by risk factor modification and surgical removal. Lesions are either excised or **ablated** (removed completely) with laser therapy. While the likelihood of malignant progression can be substantially decreased by therapeutic intervention, as many as 50% of patients will experience "recurrence." This is due to either incomplete removal of the lesion or a process known as field cancerization (see also Chapter 12 under neoplasms). The basis of this process is that carcinogens in the mouth are unlikely to affect only a localized area. Rather they are likely to produce cellular changes all over the mouth (field), even though lesions may not be clinically apparent. The altered cells can continue to progress and ultimately produce additional lesions that may appear as a recurrence of the original lesion (Feller et al., 2006). Any patient who has been treated for a premalignant lesion has a significantly increased chance of developing additional lesions over time; therefore, continued clinical follow-up is mandatory.

NAME: Oral submucous fibrosis (OSF)

Etiology: As in many conditions that are considered premalignant, OSF is believed to have a multifactorial etiology. The following factors appear to be associated with an increased risk of developing this condition: (1) areca nut or betel nut chewing, (2) genetic predisposition and genetic mutation, and (3) nutritional deficiencies.

Method of Transmission: None

Epidemiology: It is estimated that 2.5 million individuals are affected by OSF around the world. Most of the cases are found in India, Southeast Asian countries, and Pacific island nations (More et al., 2012). OSF has also become a public health issue among immigrant populations located in the United Kingdom and South Africa (Lountzis et al., 2006). OSF is rare in the United States; however, because of the significant increase in Asian immigration, OSF is currently seen more frequently in the United States than it ever has been before. The possibility of increased use has continued to rise and was at one time limited to certain countries but has become increasingly popular with youth due to flavoring agents and culture (Akhter et al., 2008).

Pathogenesis: Most cases develop in patients who chew some form of areca nut, usually betel quid, which is a form of topical tobacco mixed with slaked lime and areca nuts. Arecoline, a substance found in betel nuts, stimulates the production of collagen by fibroblasts. Other substances encourage the newly formed fibers to cross-link, enhancing their strength and inhibiting the body's attempts to break them down. Finally, studies suggest that genetic mutations occur in fibroblasts that are exposed to the chemicals in betel nut, further stimulating the production of collagen fibers. This persists even after cessation of the habit. Three stages of clinical development have been identified and are discussed below along with perioral and intraoral characteristics.

Extraoral Characteristics: None

Perioral and Intraoral Characteristics: The first stage of development involves a generalized stomatitis that manifests as erythematous mucosal tissues that develop numerous vesicles and ulcers. An increase in melanin pigmentation and oral petechia may also be noted. The second stage, or fibrosis stage, is characterized by the progressive accumulation of collagen fibers in the mucosal tissues. Fibrous bands of tissue that form in the buccal and labial mucosa result in a white marble-like appearance and cause progressive limitation in opening the mouth (trismus) (Fig. 14.29).There is decreased flexibility of the tongue, soft palate, and uvula. Problems with speech, eating, and swallowing are common. The floor of the mouth becomes leathery, and the gingiva becomes fibrotic and pale. The third stage is characterized by the formation of premalignant leukoplakia lesions in about 25% of those affected by OSF (Lountzis et al., 2006).

FIGURE 14.29. Oral submucous fibrosis (OSF). Note the white marbled appearance of the buccal mucosa. (Courtesy of Dr. John Wright.)

Distinguishing Characteristics: Patients who habitually chew betel nut have extensive dark (red or mahogany) staining of their teeth. The presence of this type of staining should prompt the dental professional to thoroughly investigate its cause.

Significant Microscopic Features: Early stages show edema, large fibroblasts, and inflammatory infiltrates. More advanced stages show dense bundles of collagen, decreased vascularity, and no edema.

Dental Implications: Patients who habitually chew betel nut should be encouraged to stop the habit, have regular oral examinations, and receive appropriate education related to the complications of OSF.

Differential Diagnosis: OSF may present with manifestations that are similar to those seen in scleroderma (see Chapter 23) and LP (see Chapters 13 and 14).

Treatment and Prognosis: There is no effective treatment for this condition, and the process is irreversible. The patient should be advised to stop chewing betel nut. Steroid injections may slow the progression of the disease. Surgery may be necessary to treat severe trismus by releasing the fibrous bands. The prognosis depends on the severity of the symptoms and whether the patient will cease chewing betel nut. The risk of developing squamous cell carcinoma within OSF is 7.6% (Lountzis et al., 2006). Supplements such as alpha lipoic acid in conjunction with intralesional steroids and hyaluronidase show promise (Rao, 2010). Lycopene and curcumin may have benefits in precancerous lesions as well (Kumar et al., 2007). Early treatment and intervention is crucial. More research is needed in meeting the educational needs related to this disorder (Kerr et al., 2011).

SUMMARY

- Fordyce granules and leukoedema are examples of white oral lesions that are considered variations of normal tissues or structures.
- Geographic tongue is an inflammatory lesion of unknown etiology that is normally asymptomatic.
- Frictional keratosis is an adaptive response to chronic physical irritation that stimulates the production of keratin within the mucosa and results in a mucosal "callus."
- Linea alba is a specific form of frictional keratosis often associated with bruxing and/or clenching.
- Cheek chewing is another example of frictional keratosis that manifests in individuals who habitually chew on their cheeks.
- Nicotine stomatitis manifests as a whitening of the palatal mucosa with inflammation of the minor salivary gland ducts resulting in erythema.
- Elongation of the filiform papillae results in hairy tongue. The etiology of hairy tongue is unknown; however, some of the risk factors associated with its development include systemic antibiotic therapy and oxygenating mouth rinses.
- White lesions caused by chemical or thermal burns are common. Aspirin is the most common cause of chemical burns, while hot food is the most common cause of thermal burns.
- Acute pseudomembranous candidiasis presents as curd-like plaques on the mucosa that can be wiped off. Immune suppression is frequently associated with this infection.
- Chronic hyperplastic candidiasis is the least common form of candidal infection. These lesions have a slight potential to become dysplastic and to undergo malignant transformation.
- Hairy leukoplakia is caused by an infection with the Epstein-Barr virus and is associated with immunosuppression due to HIV infection, medications, or other immunosuppressive conditions.
- Reticular and plaque forms of lichen planus are associated with white oral lesions. These lesions are usually asymptomatic and tend to affect the buccal mucosa.
- White sponge nevus is a rare autosomal dominant genetic disorder that manifests as white plaques, usually found on the buccal and labial mucosa.
- Leukoplakia is a white lesion that cannot be diagnosed as any other condition. These are considered premalignant lesions and are commonly associated with tobacco use.
- Oral submucous fibrosis is a premalignant condition that is associated with betel nut chewing. This condition may result in severe impairment of oral functions because of fibrosis and loss of tissue elasticity.

CHAPTER REVIEW

CASE STUDY 14.1

1. How would you describe the white lesion depicted in Figure 14.30?
   - a. Verrucous-like
   - b. Corrugated
   - c. Circumscribed
   - d. Segmented
   - e. Both a and b are acceptable
2. Which of the following would be a good step in diagnosing this lesion?
   - a. Take a digital image of the lesion for documentation and future comparison
   - b. Try to wipe the area to determine if it is *Candida albicans*
   - c. Use a device to assess malignancy—perhaps one of the cancer screening devices would help in determining whether the lesion is cancer
   - d. Determine any frictional component
   - e. All of the above are worthy diagnostic tools

FIGURE 14.30.

For answers and additional review activities, log in to thePoint.lww.com

CASE STUDY 14.2

The description of the entity in Figure 14.31 is that of a white, slightly raised tissue plaque with irregular borders. The plaque-like structure is not circumscribed and exhibits thick white foci at the most posterior border. The patient has not injured the tongue to his knowledge and is experiencing no pain. You see no sharp edges or indications that he is abrading his tongue. The patient is a nonsmoker but drinks occasionally. He believes that the white tissue has been present for several months. As you and the dentist evaluate the area, the patient tells you that he really does not believe that there is anything to be concerned about and would like to come back for a reevaluation when his next checkup occurs in 6 months. He states that he is in good health and his family physician just saw him for his annual physical and gave him a clean bill of health.

1. Given this scenario, what would be your line of reasoning and course of action to treat the patient? List the best answer given the choices below.
   - a. Have him return in 6 months.
   - b. Tell him you need to perform a biopsy.
   - c. Use an adjunctive cancer screening device.
   - d. Tell him to come back in 2 weeks.
   - e. Ask him to discontinue any alcohol and return in a month.

FIGURE 14.31.

For answers and additional review activities, log in to thePoint.lww.com

Critical Thinking Activity

A 45-year-old male patient is seen in your office today for routine prophylaxis. The patient is on a 3-month maintenance appointment schedule. As you review the notes, you read that the patient has type 2 diabetes. He has allergies and uses a corticosteroid spray for seasonal allergic rhinitis. Last visit, he was treated by your office hygienist who practices on alternate days. Her notes indicate that the patient continues to be treated for oral fungal infections several times a year.

As you perform your oral examination, you notice a moderate amount of calculus, but minimal plaque. The patient is missing 22 to 28, which is sustained by a partial denture. His third molars are missing, and all remaining molar teeth have mesial, occlusal, and distal (MOD) restorations. The oral tissue appears normal in most areas, but you notice some white patchy areas in several locations. As you read the previous notes, the same scenario existed 3 months ago. The patient was given a nystatin rinse and asked to return within a few days. Although he did not return for another evaluation, he tells you that his wife checked his mouth and reported that the areas were completely gone within a few days.

A differential diagnosis of this lesion would include many conditions; however, in this scenario, the lesion is determined to be a *Candida* infection.

You would want to let this patient know that the continued infection may be due to several factors:

1. Partners may continue to reinfect each other with *Candida albicans*
2. Corticosteroid use makes the patient more likely to develop *Candida* infection because of decreased immune function
3. The patient may not be properly disinfecting appliances or toothbrushes.

Using a psychological approach with patient management, write out the points that you would make when discussing this scenario with the patient. Consider the following:

- Written instructions are always optimal for patients newly diagnosed or those who have chronic dental problems.
- Assisting the patient in determining why reinfection occurs is a professional responsibility.
- Give the patient instructions on how to care for the toothbrush, appliances and how to disinfect these items. Brush heads and toothbrushes should be discarded when *Candida* infection occurs.

Portfolio Possibilities

- Yeast infections are commonly seen in clinical practice, especially affecting the elderly. Volunteer to visit a nursing home in your community and present a discussion on yeast infections. Design a table clinic appropriate for your audience on intraoral yeast infections. Include how patients get these infections, predisposing factors, clinical features, and management.
- Volunteer to give a presentation on the harmful effects of spit tobacco at your local high school. Organize a presentation including facts about oral cancer, the role of tobacco and spit tobacco, clinical features of cancer and their warning signs for patients, and management.

Media Menu

Web Sites

American Cancer Society—Information and resources for cancer
http://www.cancer.org/

Centers for Disease Control and Prevention: Emerging Infectious Diseases journal
http://www.cdc.go/ncidod/eid/index.htm

National Organization for Rare Diseases
http://www.rarediseases.org/

World Health Organization
http://www.who.int/en/

Study Tools

Take advantage of additional online resources to help you study and ace your exams!

- Answers to case studies in the book
- Additional case studies and answers
- Interactive quiz bank with answer feedback
- Fully searchable e-book for quick lookup and studying on-the-go
- Expanded Media Menu with direct links to related Web sites and multimedia resources
- Supplemental readings

thePoint Online resources and links are available at http://thepoint.lww.com/DeLong2e.

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Chapter 14 **LESION/CONDITION SUMMARY TABLE**

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Fordyce Granules	Normal	Sebaceous glands that are on the surface of oral mucosa	Superficial yellowish to yellow white, slightly elevated papules	Normal sebaceous glands composed of lobules of rounded cells with cleared granular cytoplasm	No treatment required	None
Leukoedema	Variation of normal	Intracellular edema producing whiteness	Whitish to blue opaque color with fine wrinkles of mucosa Bilateral; usually disappears when stretched	Thickened epithelium with cells that are vacuolated because of intracellular edema	No treatment required	None
Geographic Tongue (GT) Migratory Glossitis Erythema Migrans	Unknown	Inflammatory condition with unknown cause	Depapillated areas on the tongue. Usually appear on dorsal areas of the tongue, pink or red with concentric white to yellowish rings. The patient may complain of burning.	Tissue shows inflammatory component in connective tissue with neutrophils migrating through the epithelium, forming small microabscesses.	No treatment required, but images (digital) may be made to compare future problems and for reassurance of the patient.	Treatment should not proceed when lesions are present and any sign of exudate is noticed. Other than a burning sensation, patients are asymptomatic.
Frictional Keratosis	Physical irritation	Overproduction of keratin causing a callus that appears lighter than surrounding tissue	Whitish plaque that does not rub off	Thick keratin layer	Removal of stimulant	Removal of the irritant. In the case of a chronic self-inflicted injury, psychiatric evaluation may be needed.
Linea Alba	Localized form of frictional keratosis. Variation of normal.	Reaction to irritation	White line along the occlusal plane of the buccal mucosa	None	No treatment required	None—only recognition of the entity.
Morsicatio Buccarum and Morsicatio Labiorum	Chronic tissue trauma usually due to chewing on the cheek.	Overproduction of keratin due to chronic tissue injury	White, macerated surface resulting in chronic tissue injury	None	The patient should be encouraged to stop the habit of cheek or lip chewing.	The patient should know that chronic tissue injury is not healthy and may ultimately allow pathogens to enter the site, affecting health.
Nicotine Stomatitis	Due to heat and chemicals from heavy smoking—especially reverse smoking.	Tissue irritation from heat and harmful chemicals	Palate is white and minor salivary gland ducts are irritated, appearing red. Small elevations are evident.	None	May lead to oral cancer and should be monitored. The patient should be encouraged to cease the habit.	Smoking cessation is required.

continues

Chapter 14 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Hairy Tongue	May be found in immunocompromised indivduals and may be medication induced.	Predisposing factors: Antibiotics Radiation therapy Smoking Peroxide rinses Overgrowth of oral flora	Elongation of the filiform papillae with discolored surface on the dorsal of the tongue	None	The patient is usually concerned about the appearance of the tongue and the discoloration may be noticeable when speaking.	Debridement with toothbrush and tongue cleaner is optimal with discontinuation of contributing products such as peroxide and antifungal medication may be needed. Essential oils and chlorhexidine gluconate are recommended as well.
Chemical Burns	Generally the result of a group of chemicals or drugs that cause caustic burns to the oral tissues.	NA	White plaques of varying sizes. The covering may be removed leaving red, raw areas.	Surface epithelium showing coagulation necrosis or denuded epithelium with ulceration	Removal of the offending products.	The lesions may be confused with other pathological conditions. Education of the patient with regard to the use of medications is appropriate.
Acute Pseudomembranous Candidiasis	Caused by species of *Candida;* overgrowth of the yeast-like fungus. Altered oral environment caused by smoking, xerostomia, immune system disorders, diabetes, corticosteroid use, and antibiotics.	Newborns may contract this from the birth canal. The organism produces necrosis of the surface epithelium or produces erythema resulting from the body's reaction to the organism.	Multiple raised whitish curd-like plaques with variable erythema. Plaques can be scraped off with a tongue blade leaving a red, raw surface.	*Candida* organisms grow on the surface of the mucosa and produce necrosis of superficial keratinocytes. As cells die, they lie on the surface of the tissue as white plaques matted together by the hyphae of the organisms.	Infection is treated with antifungal medications. Review the patient's medical history for underlying systemic problems. Sometimes partners of the patient may be infected as well and may need treatment when ongoing reinfection is a problem.	Medications such as nystatin or clotrimazole troches. Systemic medications are used such as fluconazole. Denture appliances need to be treated separately, and toothbrushes should be replaced with a new one during each episode.
Chronic Hyperplastic Candidiasis (Candidal Leukoplakia)	Caused by *Candida albicans*	***C. albicans*** may stimulate a hyperplastic reaction in the mucosa tissues. Low transmission rate.	Thickened, often raised whitish plaque that does *not* rub off. Lesions commonly affect the tongue or commissure.	Hyperkeratosis, epithelial hyperplasia, and the causative hyphae of the organism in the superficial keratin	Systemic antifungals, topical application of vitamin A/retinoids and β-carotenes, laser surgery, and conventional surgical excision. Treatment is not always completely successful.	This is the only form of candidiasis that shows malignant potential. The more common forms of candidiasis such as erythematous or pseudomembranous described above do not progress to CA.

Chapter 14 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Hairy Leukoplakia (HL)	Infection from the Epstein-Barr virus (EBV)	Linked to immunosuppression and HIV	Bilateral white plaques along the lateral border of the tongue that do not rub off. Appear as vertical or raised ridges.	Hyperkeratosis with exophytic extensions that appear somewhat like hair	Antiviral therapy but recurrence is very possible	Very important dentally since it is an indicator of progression from HIV status to full-blown AIDS. Does not have malignant potential in and of itself.
Parulis	Odontogenic infection	Purulent exudate accumulates in specific area	Raised lesion with exudate of white or yellow color	Evidence of pus and infection	Tooth is treated and antibiotics may be needed to fight infection. Drainage may be needed.	Evidence of infection and the source needs to be treated.
Lichen Planus	May be autoimmune but to date no antigen has been found. Many feel it is premature to classify as autoimmune.	Lymphocytes that target the basement membrane and eventually liquefy	White, lacy lines called Wickham striae are notable. May also be erythematous, shiny red gingival tissue. Highly friable. Painful and prone to chronic sloughing.	Basal cell liquefaction. Inflammatory lymphocytic infiltrate. Immunofluorescence needed to confirm. Band-like lymphocytes at the basement membrane. "Sawtooth" appearance of the rete ridges.	Steroids. Careful selection of nonabrasive toothpaste with limited flavoring agents. Foods may cause burning and spicy foods cause pain in some patients.	Careful, low-trauma dental treatment. The tissues are highly susceptible to stripping. Air polishers and abrasive materials should not be used. Low-level ultrasonic or hand instruments. Lichen planus may affect any lining mucosa including the genitals and the esophagus.
White Sponge Nevus (WSN)	Inherited condition caused by mutation of certain keratin genes	Autosomal dominant trait. A diagnosis is made rapidly with a family history.	Widespread keratinization of the buccal mucosa and the labial mucosa.	Hyperkeratosis, acanthosis, and cytoplasmic clearing of the epithelial cells	Once confirmed, no treatment is needed and prognosis is excellent.	The patient may be sensitive to appearance of the white tissue.
Leukoplakia	Descriptive term for any white patch or plaque. Usually from tobacco use related to cigarette smoking or topical tobacco use.	The term is nonspecific for any disease state. After other disease possibilities have been ruled out, the term leukoplakia is used. It is considered premalignant.	The term is also a diagnosis by exclusion. The lesion may be white (leukoplakia) or red (erythroplakia). Epithelial dysplasia may occur.	Hyperkeratosis, with or without acanthosis. Dysplasia and carcinoma in situ may be visible in 20% of leukoplakias. High-risk areas have higher rates of malignancy. The floor of the mouth has a 40% chance of the leukoplakia being either dysplasia or CA.	Biopsy should be performed. Discontinuing alcohol and tobacco use. Nutrition, stress reduction, and lifestyle interventions are important in reducing further occurrence. Recurrence may be noted in dysplastic lesions.	The site of a leukoplakia may determine the risk for progression to oral cancer. High-risk areas are known to progress and should be monitored cautiously. The patient should be followed and biopsied if future lesions are observed.

continues

Chapter 14 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Oral Submucous Fibrosis (OSF)	Areca nut, tobacco use, betel nut chewing. Genetic predisposition and nutritional deficiency.	Use of areca nut products, betel quid, and other products that cause tissue changes.	Stomatitis, ulcers, vesicles, and discoloration. Fibrous bands occur producing a white-lined, marble-like appearance. Decreased flexibility of the tongue and the opening to the mouth.	Edema, large fibroblasts, and inflammatory infiltrates. Dense bundles of collagen, decreased vascularity, and no edema.	Nutritional counseling, discontinuing the use of the products, surgery may be needed, steroid injections, and new data suggest alpha lipoic acid and hyaluronidase. Both lycopene and curcumin may have benefits as well. Antioxidants and polyphenols are anti-inflammatory agents found in food groups that show promise.	SMF is a premalignant disease. Discontinuing the products is needed along with careful monitoring.

CHAPTER 15

Pigmented Lesions

KEY TERMS

Amalgam tattoo
Amelanotic melanoma
Argyria
Basal keratinocytes
Biologic therapy
Blue nevus
Compound nevus
Ephelis (pl., ephelides)
Focal argyrosis
Focal melanosis (oral melanotic macule)
Intradermal nevus
Intramucosal nevus
Junctional nevus
Labial melanotic macule
Laugier-Hunziker syndrome
Lentigo maligna
Melanin
Melanocytes
Melanosis
Minocycline tissue staining (black bone stain)
Nevus
Oral melanoma
Oral submucous fibrosis (OSF)
Physiologic pigmentation
Plumbism
Quid
Smoker's melanosis (smoking-associated melanosis)
Solar lentigines (solar lentigo)

LEARNING OUTCOMES

1. Define and use the key terms in this chapter.
2. List three pigmented lesions that are physiologic and three pigmented lesions that are pathologic.
3. List three factors that contribute to the pigmentation of oral tissues.
4. Name six important factors that assist in a differential diagnosis of pigmented lesions.
5. Discuss the three origins of traumatic or inflammatory lesions.
6. Name two systemic diseases that may have pigmentation of the tissues as a sign of the actual disease.
7. Name four diseases involving an inflammatory process, which sometimes produces pigmentation.
8. Name four medications that may cause oral pigmentation.
9. List two diseases that may produce pigmentation of the lips.
10. Name three heavy metals that exhibit pigmentation of the tissues.
11. Discuss the types of antibiotics that may cause pigmentation of the oral tissues.

CHAPTER OUTLINE

Variations of Normal
- Physiologic pigmentation

Traumatic or Inflammatory Lesions
- Amalgam tattoo

Other Metal Pigmentations
- Titanium Implants
- Intentional Tattooing
- Heavy Metal Pigmentation

Pigmentation Associated with Drugs
- Minocycline tissue staining
- AZT (azidothymidine or Retrovir)
- Smoking-associated melanosis
- Betel Quid Use

Congenital or Genetic Disorders
- Nevus
- Oral melanotic macule

Disease-Associated Melanosis
- Laugier-Hunziker syndrome

Neoplasms
- Oral melanoma

RELATED CLINICAL PROTOCOLS

#11 Patient Education: Oral Cancer Self-Examination
#24 Tobacco Cessation
#25 How to Utilize Nutrition Counseling in Practice
#26 Helping Relationships for Dental Hygienists
#27 Motivational Interviewing for Behavior Change

Pigmented lesions may be physiologic or pathologic. Some are considered to be benign and some are extremely malignant. In early stages of both physiologic and pathologic lesions, it is often difficult to determine the seriousness of the lesion simply by a clinical examination. When a direct cause of a lesion cannot be determined, further investigation is always warranted, including a biopsy with microscopic examination of the tissue. In these cases, a thorough clinical examination and a full medical history of the patient are very important. Knowing the medical history of the patient, the medications that are being taken, and the lifestyle of the individual is crucial in determining the pathogenesis of any lesion. The duration, location, clinical appearance, radiographic appearances, pathology reports, and self-reported changes are all important in the differential diagnosis. These steps are needed to distinguish a benign lesion from a malignant one. Another important factor related to a change in a lesion is the reality that, very often, what begins as a benign lesion takes a radical course into malignancy. Therefore, any changes in the state of a lesion should be taken seriously.

In this chapter, we explore the color variations of normal tissue versus tissue that has undergone pathologic changes. Some areas of pigmentation are localized, such as a benign amalgam tattoo. However, the early stages of the most malignant lesion, a melanoma, can also be localized and have a clinical appearance similar to that of an amalgam tattoo. Pigmented areas may be generalized, such as genetic and racial pigmentation, or they may be related to endocrine disorders, pregnancy, inflammatory conditions, trauma, or medications. All of the above may cause color variations. Pigmentation may also be due to the numbers of **melanocytes.** Melanocytes are found in or at the basal (deepest) layer of the epidermis and have long dendritic extensions that extend to the keratinocytes in the more superficial layers of the epidermis. The main function of melanocytes is to protect the skin from harmful ultraviolet rays by producing **melanin,** the black or brown substance that imparts color to the skin. Each melanocyte is able to produce granules of pigment called *melanosomes* that are then transferred along the dendritic processes to the keratinocytes, thereby coloring these cells. Hormones and genetics influence the amount of melanin and pigmentation produced. Additionally, the introduction of exogenous materials into the surrounding tissues may cause a pigmented lesion. An example of pigmentation due to an exogenous material is the pigmentation that occurs when amalgam fragments become embedded within the tissues. Another example is an embedded lead pencil point that may be incurred when a child puts the pencil in his or her mouth and falls, leaving the lead point or particles within the tissue.

Essentially, oral pigmentation is due to the following:

1. The number of melanocytes
2. The amount of melanin produced
3. The incorporation of a foreign substance introduced into the oral and perioral tissues.

Variations of Normal

Color changes in the mucosa depend upon the normal pigmentation of the skin, which may appear in varied hues depending upon racial and genetic factors. Racial pigmentation occurs to some degree in all ethnic groups and is due to an increase in melanin production, not to an increase in the number of melanocytes. Therefore, dark- and light-skinned individuals have a comparable number of melanocytes, with darker-skinned individuals producing more melanin than their lighter counterparts.

NAME: Physiologic pigmentation

Etiology: Physiologic pigmentation is usually found in the gingiva, but can occur throughout the mouth. Increased pigmentation may occur during pregnancy because of the increased levels of various hormones produced. Some pigmentation may occur in postmenopausal women taking hormone replacement therapy (HRT).

Method of Transmission: Not applicable

Epidemiology: There is no sex predilection or age preference related to physiologic pigmentation, and it may occur in any age group. Physiologic pigmentation is found most often in darker-skinned individuals. Approximately 5% of whites are reported to have physiologic pigmentation.

Pathogenesis: Physiologic pigmentation occurs in certain individuals because of the tendency to produce melanin in varying amounts. The more production that occurs, the deeper the color, and depending upon the ethnicity of the individual, the color of the tissues will vary. Just as the sun causes injury to the tissue, forcing us to produce more melanin and over time giving us tanned skin, the melanin production can occur in isolated areas, producing a focal pigmented area of tissue.

Extraoral Characteristics: Some pigmentation can occur extraorally and may be associated with disease states and with a genetic predisposition. These are discussed later in this chapter. Physiologic pigmentation may extend into the lip area as is seen in Figure 15.1A, which depicts the normal melanin pigmentation of a black male. Note the inner lip pigmentation as well as the pigmentation around the gingival margin of tooth 26.

Perioral and Intraoral Characteristics: Oral melanin pigmentation may range from brown or black to dark blue. The deeper pigmentation is usually black. Figure 15.1B represents the physiologic pigmentation of the tongue. Figure 15.1C depicts the color variations in gingival tissue due to physiologic pigmentation.

Distinguishing Characteristics: Physiologic pigmented lesions do not blanch because they are due to melanin production and not to blood pooling within the tissues as a vascular pigmentation produces. In addition, the pigmentation is not caused by excess blood within a focal area such as the hematoma, ecchymosis, or petechiae that were discussed in Chapter 13.

Significant Microscopic Features: There is an increase of melanin pigmentation in **basal keratinocytes.** Melanin is also found in the connective tissue because of the dendritic processes of the melanocyte and the transfer of the melanin. A histologic section shows increased melanin in the epidermis, with unaltered numbers of melanocytes.

Dental Implications: Some patients complain about the cosmetic factors related to physiologic pigmentation when pigmentation is noticeable such as on the gingiva or perioral tissues. The tongue and gingiva may be visible when speaking and the appearance may be troublesome to the patient.

Differential Diagnosis: Pigmentation due to a serious disease should always be considered, such as the following:

1. Peutz-Jeghers syndrome, Chapters 10 and 15
2. Addison disease, Chapter 7
3. Melanoma, Chapters 5 and 15

A

B

C

FIGURE 15.1. A. Physiologic pigmentation of the inner lip and gingival margin. **B.** Physiologic pigmentation of the tongue. **C.** Physiologic pigmentation of the gingiva.

APPLICATION 15.1

When a pigmented area is noticed anywhere in the mouth, several steps should be followed to determine the etiology of the area in question:

1. Is the pigmented lesion location one that follows the pattern of a specific known lesion? An example is a blue-black area that is adjacent to an amalgam. The likely diagnosis would be an amalgam tattoo. A blue-black lesion in the palate would not follow the normal pattern or location of an amalgam tattoo.
2. Is the lesion vascular or nonvascular? Does the lesion blanch? If the lesion does not blanch (using diascopy), the clinician categorizes the lesion as nonvascular.
3. Is the lesion erosive or does it have the appearance of an inflammatory lesion? Again, the lesion would be categorized as inflammatory or noninflammatory.
4. Does the health history indicate a disease state that might produce pigmented oral lesions such as Addison disease or Peutz-Jeghers disease?
5. Does the patient know that the lesion is present? If so, further questioning may lead to a more definitive diagnosis. A childhood pencil injury in the palate is a prime example that may be discovered when fully questioning the patient.
6. If a radiograph has been taken, is there evidence in the radiograph, such as radiolucent spots suggesting metal fragments?
7. Do you have a photograph that was taken previously to offer a comparison?
8. Is there documented evidence of the previous size or shape of the lesion?
9. Upon questioning the patient, is there anything in the health history that would warrant the investigation of any disease states?
10. Are you able to confirm the cause of this lesion?
11. Is referral for a biopsy needed? Is follow-up recommended?

Treatment and Prognosis: The prognosis is excellent, and no treatment is required once a definitive diagnosis is confirmed. If the diagnosis is not clear and a clinical diagnosis cannot be made because the pigmentation does not exhibit the usual characteristics, further evaluation is needed. Follow-up should be performed when any changes occur that would require further examination.

Traumatic or Inflammatory Lesions

Traumatic lesions occur because of injury to the tissues, such as amalgam that becomes embedded in the tissues during the restoration of a tooth, which produces a dark hue. Inflammatory pigmentation occurs because of chronic injury and assault to the tissue through the use of certain medications, chronic inflammation, or thermal changes. Certain chronic inflammatory diseases cause the body to react to constant injury or assault on the tissue by producing pigmentation. An example is the pigmentation sometimes produced because of chronic inflammation caused by oral lichen planus. Another example is the pigmentation caused by constant trauma to the tissue due to the heat and chemicals associated with smoking that result in **smoker's melanosis.**

Along with the common ways mentioned above, pigmentation may also occur from intentional incorporation of metallic particles used by some cultures as esthetic enhancement of the individual. Mani (1985) reported three cases of Ethiopian women who had tattooing of the upper gingivae performed as a traditional practice. Figure 15.2A shows intentional pigmentation, performed in childhood, of a 30-year-old female from Ethiopia. In certain cultures, this practice occurs routinely and may be repeated throughout life. Tattooing of males is also practiced, but in this geographic location of Ethiopia, it is confined to the canines for males, with more extensive gingival tattooing for the females. Intentional tattooing of this nature is performed in early childhood by using soot and abrasion of the tissue until the soot is embedded within the skin. This is accomplished after multiple attempts at abrasion and layering of the pigments. In cases presented by Rawal et al. (2007), a patient reported having the placement of

FIGURE 15.2. A, B. Ethnic tattoo. (Courtesy of Dr. Doron Aframian.)

pigments performed at age 6 with a second replacement at age 10. The authors also reported a woman from Dakar, Senegal, having pigments placed at age 40 in a dental office. The patient decided to have the procedure much later in life since she did not have the customary pigmentation early in childhood. Those performing cultural tattooing from the woman's community brought in the pigments that could be placed while she had anesthesia administered.

Figure 15.2B depicts a 60-year-old woman from Arabia who has a tattoo on the lip, used to guard against bad luck. When these pigmented areas are viewed outside of the cultures in which they are performed, misdiagnosis may occur and they may be mistaken for more serious pathology. A strong cultural propensity to adapt to community standards remains, promoting the ethnic beliefs of those around them. As more hygienists treat a varying array of cultures, the probability of encountering cultural tattoos is much greater than in decades past.

The hygienist may observe a small oral tattoo on the lip, palate, or buccal mucosa caused by India ink or a graphite pencil. These unintentional tattoos are usually the result of childhood trauma and are most often caused by the child falling with a pen or pencil held in the mouth. Additionally, metal dust, broken dental burs, and any type of metal embedded into the tissue (such as titanium) may cause pigmentation through the release of ions. Several types of pigmented lesions are discussed in more depth in this section.

NAME: Amalgam tattoo (focal argyrosis)

Etiology: **Amalgam tattoos** occur because of amalgam particles becoming imbedded within the tissue.

Method of Transmission: Not applicable

Epidemiology: Amalgam tattoos may occur in all age groups, and there is no sex predilection.

Pathogenesis: Fragments of amalgam can become embedded within the tissues in several ways: Preparation of the tooth sometimes forces the particles down into the tissue; particles left in the surrounding areas could be driven down into the tissues by floss, routine tooth brushing, or scaling and polishing procedures. Additionally, endodontic procedures performed using amalgam can force the material into the tissues, and amalgam can fall into fresh extraction sites.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: The metal fragments are usually embedded in the surrounding tissue during tooth restoration or extractions. The clinical appearance of the amalgam tattoo remains within the areas that have been previously treated or in open wound areas. Therefore, you would expect to see the amalgam tattoos adjacent to a placed amalgam, in previous restorative sites, or in a previous extraction site. Occasionally, the patient may have embedded amalgam fragments in uncommon areas, such as the buccal mucosa or floor of the mouth. In these cases, the tissue becomes ulcerated or possibly has suffered an iatrogenic laceration during a dental procedure, allowing the fragments to become embedded in these unusual areas through breaks in the tissue.

The amalgam tattoo is diagnosed through both clinical appearance and radiographic appearance. Amalgam tattoos are usually localized, involving the gingiva and rarely the floor of the mouth. Since the tattoo is adjacent to previous amalgam restorations, the area that is involved is closer to the restoration and not in areas such as the floor of the mouth. The amalgam tattoo is localized and gray to blue/black and is found primarily on the gingivae and in areas next to restorative material. Confirmation can often be made with radiographs, and amalgam fragments may be seen on a radiograph.

Figure 15.3A shows an amalgam tattoo on the lower left gingiva. Figure 15.3B depicts amalgam fragments seen radiographically. Figure 15.3C depicts an amalgam tattoo in the retromolar area where amalgam entered the surgical site in the 2nd and 3rd molar region. Figure 15.3D shows amalgam fragments seen radiographically, and Figure 15.3E depicts an amalgam tattoo in the gingival tissue between the central and lateral teeth.

Distinguishing Characteristics: Opaque fragments of metal are apparent in radiographs where an amalgam tattoo is suspected and often confirm the diagnosis.

Significant Microscopic Features: Amalgam fragments embedded within the tissue specimen may be viewed through the microscope. Depending upon the age of the tattoo and the size of the discolored area, the fragments may be either focally located or dispersed throughout the specimen. Figure 15.3F depicts the histology of an amalgam tattoo. Particles of amalgam are evident, presenting as dark, opaque fragments.

Dental Implications: The cause of any pigmented area should be determined to rule out serious pathology such as melanoma.

Differential Diagnosis: Early melanomas can sometimes be mistaken for amalgam tattoos, and this mistake has grave consequences for the patient. Further investigation is always warranted to rule out malignancy when there is any doubt regarding the cause. Other considerations include:

1. Nevus, Chapter 15
2. Melanoma, Chapter 15
3. Cultural tattoos, Chapter 15

Treatment and Prognosis: No treatment is indicated for an amalgam tattoo, and the prognosis is excellent. The dental professional should document the location and clinical description of the tattoo and confirm the cause.

Other Metal Pigmentations

Metals can accumulate within the oral soft tissues as a result of either intentional or nonintentional systemic exposure

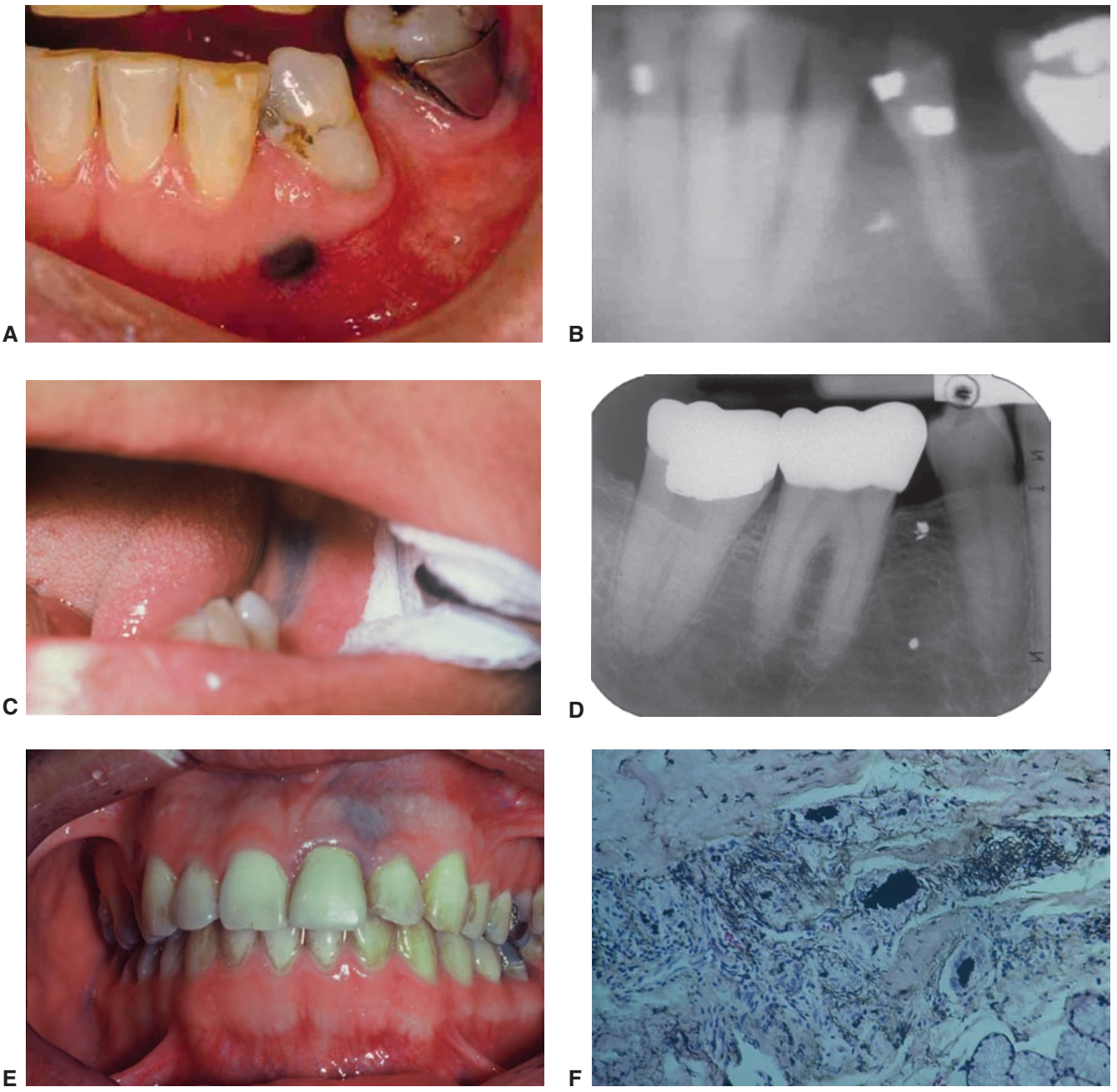

FIGURE 15.3. **A.** Amalgam tattoo. (Courtesy of Dr. William Carpenter.) **B.** Amalgam tattoo seen on radiograph. (Courtesy of Dr. William Carpenter.) **C.** Amalgam tattoo. (Courtesy of Dr. Peter Jacobsen.) **D.** Radiographic appearance of amalgam tattoo. **E.** Amalgam tattoo. (Courtesy of Dr. Peter Jacobsen.) **F.** Histologic appearance of amalgam. (Courtesy of Dr. John Jacoway.)

or localized implantation. Some of these accumulations, such as the heavy metal pigmentations, are not seen very often anymore; others, such as titanium pigmentations, will become more common.

Titanium Implants

Implants have been placed for more than two decades, and the use of implants has become commonplace. Pigmentation of the oral tissue has been reported with regard to titanium plates used in maxillofacial surgery and with orthopedic implants. Titanium ions have been reported to cause some reactions and the ions have been reported to have been found in the body. Titanium is used in devices such as pacemakers, automatic implanted cardioversion devices (AICDs), and joint replacement and dental implants (Rees, 2011). Breen and Stoker (1993) and Torgersen et al. (1995) have reported black staining from metallic wear and metal particles. Figure 15.4 depicts a patient who has multiple implants that have been in the mouth for 10 years or more. Note the gray-blue tissue around the gingiva and in the papillae from the canine to the first molar.

FIGURE 15.4. Titanium tattoo. (Courtesy of Dr. Terry Rees, Baylor College of Dentistry.)

FIGURE 15.5. Intentional tattoo. (Courtesy of Dr. Kurt Summersgill.)

The tissue has a blue cast with some pigmentation occurring in the papillae area as well as around the crown. A blue-gray discoloration of tissue adjacent to titanium dental implants has occasionally been observed, apparently resulting from the accumulation of titanium ions in the tissue. The same phenomenon may account for some pigmentation found adjacent to dental amalgams, even though larger amalgam fragments may not be seen radiographically. Additionally, titanium dust may have been released during the original preparation of the crown for the implant. The titanium dust or particles may become dispersed through the tissue in differing degrees and exhibit the blue pigmentation that is present in Figure 15.4. Recent studies have reported cases of squamous cell carcinoma (SCC) around some dental implants in patients who have at least one known risk factor for SCC. Failing implants should be evaluated to rule out the presence of malignancy disguised as peri-implant disease (Czerninski et al., 2006). Additionally, abnormal appearances may indicate an existing problem, and the implant area should be watched carefully. Any ulceration or severe pigmentation may be a warning sign of further problems.

Intentional Tattooing

Occasionally, the practitioner will find a patient who has had an oral tattoo. The patterns used may be objects or designs. Often a prime area for these tattoos is the oral vestibule tissue, since this area provides a flat, wider surface. Intentional tattooing is accomplished by using tattoo pens on the external surfaces of the body. Oral tattooing is less common than tattooing skin surfaces and often tissue piercing is involved as well. Figure 15.5 depicts a person who tattooed himself while viewing the area in a mirror, as evidenced by the inverted "N" seen in the lettering.

Heavy Metal Pigmentation

Heavy metal pigmentation occurs with exposure to various types of heavy metals such as arsenic, bismuth, platinum, lead, silver, copper, and mercury; it can be problematic in the body and may cause pigmented lesions in the soft tissues. These are rarely seen because safety practices and regulations limit the use of heavy metals in the workplace and at home, but they should be considered in a differential diagnosis of a pigmented lesion. Subjection to these metals through excessive ingestion, inhalation, or prolonged cutaneous exposure may result in pigments accumulating in the oral mucosa or in any cutaneous surface. Recently, studies have implicated silver nanoparticles used in home products, health products, medicinal applications, pesticides, and electronic devices (Yong Soon Kim et al., 2010) as collecting within the tissues. The lungs and liver were especially noted as target organs. Blood tests are always needed to determine the extent of the heavy metal accumulation in the body, and other procedures are needed to determine the amount of physical damage that the metals may have caused. Differential diagnoses include

1. **Argyria.** Argyria is the slate-gray or bluish discoloration of the skin caused by the accumulation of silver salts in the tissues. Silver was often used in the treatment of the nose and sinuses. Several metals are seen clinically as pigmentations and line stains. Discontinuing exposure to the metal is paramount. The prognosis is good when exposure is discontinued and the body levels of the substance are not high.
2. **Lead**. Lead poisoning in children, or **plumbism,** has been a significant problem in past decades and is usually due to environmental causes such as chipping paint, putty, plaster, pesticides, and lead-lined pipes. Lead-line stain, sometimes referred to as Burtonian line, is often seen at the gingival margins when the lead proportion reaches certain levels. The common color of the line, often found in the premolar and molar gingiva, is blue, gray, or black. Figure 15.6 shows lead-line stain along the gingival margins.
3. **Bismuth**. Bismuth was used to treat syphilis and produces a thin blue-black line. Diascopy may be used to differentiate heavy metals from common gingivitis around the margins. The lead line will become more accentuated when a glass slide is placed over the tissue,

FIGURE 15.6. Lead-line stain. (Courtesy of Dr. Peter Lockhart, Carolinas Medical Center, Department of Oral Medicine.)

and the gingivitis line (due to inflammatory causes) will disappear (Lockhart, 1981). Further testing to confirm lead accumulation or differentiation from other heavy metals is needed, with blood levels documented. Recent reports of macular pigmentation of the tongue were related to bismuth subsalicylate (Pepto-Bismol) as the suspected agent responsible for the black tongue in a patient (Cohen, 2009).

Pigmentation Associated with Drugs

Oral pigmentation is associated with certain medications such as minocycline, tetracycline derivatives, azidothymidine (AZT), some oral contraceptives, hormone replacement medications, bleomycin, busulfan, clofazimine, and antimalarial medications. A wide range of such medications exists, with varying amounts of pigmentation produced. See Box 15.1 for a more extensive list of these medications and other substances.

NAME: Minocycline tissue staining (black bone staining)

Etiology: Minocycline tissue staining, or black bone staining, is caused by ingestion of minocycline, a semisynthetic tetracycline that was introduced in the 1960s. The medication is used in the treatment of acne and other inflammatory and immune-mediated diseases. Since minocycline is a broad-spectrum antibiotic, it can be used in a wide variety of diseases. When used in the treatment of acne, it may be prescribed for long periods to treat the skin disorder. Dark staining of hard and soft tissues is associated with the medication when used long-term. Studies suggest staining may occur not only with minocycline, but with other tetracycline-based medications as well. The oral manifestations of tetracycline staining have been well documented (Sanchez and Rogers, 2004; Westbury and Najera, 1997; Rumbak et al., 1991).

Method of Transmission: Not applicable

BOX 15.1 Drugs and Other Substances Causing Oral Pigmentation

- Tobacco-related pigmentation
  - Nicotine products
  - Betel quid with tobacco
- Addiction and "socially used drugs"
  - Heroin
  - Bark and seed chewing
- Heavy metals
  - Lead
  - Gold (chrysiasis)
  - Silver (argyria)
  - Arsenic
  - Titanium
- Hormone-related medications
  - Oral contraceptives
  - Hormone replacement therapy—Premarin
- Antibiotics[a]
  - Tetracycline
  - Minocycline
- Antimalarials
  - Quinidine
  - Chloroquine
- Antitumor agents
  - Busulfan (leukemia)
  - Bleomycin
  - Cyclophosphamide
  - Nitrogen mustard
- Medications used for specific diseases
  - Zidovudine, AZT (antiviral treatment for AIDS)
  - Ketoconazole (*Candida* infections, histoplasmosis)
  - Clofazimine (leprosy)
  - Amiodarone HCL (antidysrhythmic)

[a]Cephalosporins and penicillins may cause brown-black hairy tongue pigmentation due to *Candida* growth.

Epidemiology: All age groups are affected; however, related staining is found more often in younger adults, since the medications are prescribed frequently in this age group for the treatment of acne. There is no sex predilection.

Pathogenesis: Depending upon the medication, different sites may be affected orally and periorally. The alveolar area and bone areas of the gingiva (hard palate and attached gingiva) are affected most often with long-term use of minocycline. The staining occurs because of the accumulation of elements of the medication in the bone or the roots of the teeth that darken their color and thereby impart a darker color to the overlying tissues. These same elements can accumulate in soft tissues, also causing diffuse staining or deeper coloration.

Extraoral Characteristics: The sclera may become hyperpigmented, and the nail beds can exhibit staining as well. Pigmentation has been reported in other tissues such as the thyroid and the skin.

Perioral and Intraoral Characteristics: Minocycline pigmentation appears as generalized darker pigmented areas in the alveolar, palatal, and vestibule areas. Depending upon the severity of the staining, the lips may appear slightly darker or pigmented. Figure 15.7 depicts the accumulation of

FIGURE 15.7. Minocycline—black bone staining. (Courtesy of Dr. Michael Brennan.)

FIGURE 15.8. Pigmentation on the tongue from the use of AZT in the treatment of AIDS. (Courtesy of Dr. Terry Rees.)

minocycline in the mucosa and bone, with a darkened area reaching the vestibule. The teeth exhibit a blue-gray color that is typical with this type of medication.

Distinguishing Characteristics: Minocycline staining manifests clinically as black to brown staining that may be focal or generalized throughout the tissue toward the roots of the teeth.

Significant Microscopic Features: The typical microscopic features are fine brown spherical pigmented granules within the specimen.

Dental Implications: Minocycline that is prescribed for skin conditions over months or years may also affect the teeth and the oral mucosa. Patients may request bleaching and cosmetic dental procedures, depending upon the severity of the discoloration.

Differential Diagnosis: Physiologic pigmentation and disease states such as Addison disease, melanoma, and Peutz-Jeghers syndrome may have appearances similar to those of drug-induced pigmentation such as minocycline staining.

Treatment and Prognosis: No treatment is needed, but discontinuing the medication when possible would diminish further staining. The prognosis is good when the medication is discontinued and further staining is not permitted.

AZT (azidothymidine or Retrovir)

The buccal mucosa, tongue, palate, and nail beds may be affected with the use of azidothymidine (AZT) for the treatment of AIDS. AZT may cause nail pigmentation in addition to mucosal-pigmented areas such as those shown in Figure 15.8, which depicts heavy pigmentation of the tongue of a patient taking AZT for the treatment of AIDS.

NAME: Smoking-associated melanosis

Etiology: **Smoking-associated melanosis** (smoker's melanosis) is caused by the use of tobacco products that stimulate the production of melanocytes within the tissue. Melanin functions as a defense mechanism against toxic agents penetrating the oral mucosa. Tobacco may be used in many different forms and is most often smoked or chewed. Tobacco contains known carcinogens, and its relationship to oral cancer is well documented.

Method of Transmission: Smoking-associated melanosis is not contagious, since it is tobacco related.

Epidemiology: A higher percentage of women, especially those using contraceptives, are associated with smoker's melanosis. This is due to the increased hormone level associated with the development of melanosis in women. Any age group may be affected.

Pathogenesis: Smoking-associated melanosis is related to a component in tobacco that stimulates melanocytes to produce melanin. Since melanin is produced as a protective mechanism, toxic substances cause melanin to be produced to protect the tissue from heat and toxins. Most areas of the mucosa, gingiva, and palate can be affected. Women in childbearing years are more affected, supporting the role of a hormonal influence in the degree of pigmentation.

Extraoral Characteristics: Depending upon the degree of pigmentation, the lips may be affected, and the perioral tissue at the wet line of the lips may be involved. Existing physiologic pigmentation may be deepened as well.

Perioral and Intraoral Characteristics: Usually, light pigmentation occurs with the labial gingiva since this is a target region. The degree of pigmentation is associated with the amount of tobacco used and the physiologic component of the individual. Figure 15.9 shows smoking-associated melanosis, with the soft palate exhibiting the characteristic light brown pigmentation that is diffuse through the area. The tongue is also pigmented a soft brown with elongation of the filiform papillae. Both chemicals and heat are a factor in the accentuated papillae evident in Figure 15.9.

Distinguishing Characteristics: The pigmentation that is produced has a diffuse, light brown color. Other disease states might have a similar appearance; therefore, careful

FIGURE 15.9. Smoking-associated melanosis of the soft palate with tongue pigments.

consideration of other possibilities and health states is very important in a final diagnosis.

Significant Microscopic Features: Increases in melanin production are evident in basal keratinocytes. The microscopic appearance is similar to that seen in physiologic pigmentation.

Dental Implications: Any tobacco product use increases the risk of oral cancer. Careful follow-up with the patient is crucial, and the patient should be educated about oral cancer and taught to do an oral cancer self-screening examination (see Clinical Protocol #11). Smoking cessation should be recommended by the hygienist or the dentist and included in a treatment plan for discontinuation of all tobacco products (see Clinical Protocol #24 for smoking cessation rules and medications used in stopping smoking; see also Clinical Protocol #27 for motivational interviewing). If the office does not have a smoking cessation program, the patient should be referred to a special smoking cessation clinic. Many such clinics are associated with dental schools, hospitals, and private individuals. See Box 15.2 for a list of existing clinics and programs that enable the clinician to become certified as a tobacco treatment specialist. Also listed in Box 15.3 are phone apps that assist the patient in finding resources for smoking cessation.

Differential Diagnosis: The following disease states have similar pigmentation appearances and should be considered:

1. Peutz-Jeghers syndrome, Chapter 10
2. Physiologic pigmentation, Chapter 15
3. Addison disease, Chapter 10
4. Laugier-Hunziker syndrome, Chapter 15
5. Medication induced, Chapter 15

Treatment and Prognosis: Smoking cessation is the most appropriate treatment. Discontinued use of tobacco products results in less pigmentation and, finally, resolution in most cases. The prognosis is excellent when the patient stops using tobacco products. Long-term tobacco use in any form dramatically increases the patient's chance of oral cancer. Additionally, this risk increases when coupled with alcohol use.

Betel Quid Use

Tobacco is used in other forms, many of which have cultural origins. Tobacco is often combined with additional products, placed in a betel leaf becoming what is called a **"quid."** The term *quid* refers to a mixture of substances placed in the mouth and remaining in contact with the mucosa, usually containing one or both of the two basic ingredients, tobacco or ground areca nut, in raw or any manufactured or processed form (Zain et al., 1996). Areca nut contains the substance arecoline. When coupled with slaked lime, tobacco, and other products, they stimulate the production of collagen by fibroblasts, and chronic use causes cross-linking of the newly formed fibers. The body cannot break these down, and they continue to strengthen. Constriction of the tissues occurs and, over time, limits the oral opening.

The betel quid is considered a specific variety of quid that uses the betel leaf. Usually, there is a mixture of areca nut, slaked lime, catechu, several condiments such as flavoring agents, and often tobacco, wrapped in a betel leaf. Figure 15.10A depicts the ingredients used in a betel quid. The ingredients are placed on the leaf and then rolled into a quid. Figure 15.10B shows a finished quid.

Additionally, combinations of these products with or without tobacco may be used; some may be in the form of quid and others may be chewed, smoked, or rubbed into the oral tissues. Residents in Asia, Taiwan, Papua New Guinea, India, and neighboring countries commonly practice the use of these products. The quid is placed in the mouth and held for extended periods. Quid is addictive and produces a sense of euphoria. The practice is culturally driven as well. When coupled with alcohol use, a person's chance of oral cancer is increased (Nair et al., 2004). A quid-induced lesion is associated with pigmentation, usually observed after long-term use and sometimes after only brief encounters with the products (Sarswathi et al., 2003). Tobacco with lime, betel quid with tobacco, betel quid without tobacco, and areca nut have been classified as carcinogenic to humans. Recent studies by Kerr et al.

BOX 15.2

National Contact Information and Smoking Cessation Clinics

Organizations

American Cancer Society (800) ACS-2345
www.cancer.org

American Heart Association (800) 242-8721
www.heart.org

American Lung Association (800) 586-4872
www.lung.org/stop-smoking/

Centers for Disease Control
www.cdc.gov/tobacco
www.cdc.gov/tobacco/how2quit.htm

The Oral Cancer Foundation
www.oralcancerfoundation.org
www.oralcancerfoundation.org/tobacco/index.htm
www.oralcancerfoundation.org/dental/role_of_dentists.htm

The World Health Organization
http://www.who.int/tobacco/en/

U.S. Department of Health and Human Services
www.hhs.gov/safety/index.html

National Institutes of Health
www.nih.gov

U.S. Department of Health & Human Services Office of the Surgeon General
www.surgeongeneral.gov/tobacco/

Agency for Healthcare Research and Quality
www.ahrq.gov/consumer/helpsmok.htm

American Legacy Foundation
www.legacyforhealth.org

Association for the Treatment of Tobacco Use and Dependence (ATTUD)
www.attud.org/

National Cancer Institute (800) 422-6237
www.cancer.gov
www.cancercontrol.cancer.gov/tcrb/resources.html
www.cancer.gov/cancertopics/tobacco/smoking
www.cancer.gov/cancertopics/smokeless-tobacco

Oral Health America-NTEP 312-836-9900
info@oralhealthamerica.org
www.oralhealthamerica.org

Internet Resources

Smoking Resources
www.quitnet.com
www.webmd.com
http://quitworks.makesmokinghistory.org/
www.yesquit.com
www.smokefree.gov
www.becomeanex.org
www.venomocity.com
www.nicotine-anonymous.org

North American Quitline Consortium
www.naquitline.org

Smokeless Resources:
www.killthecan.org
www.nstep.org
www.chewfree.com
www.MyLastDip.com
www.entnet.org
www.outrageavenue.com

American Dental Hygienists' Association in partnership with the Smoking Cessation Leadership Center
http://www.askadviserefer.org

Medical and Dental Schools Providing Smoking Cessation Clinics and [a]Training for Professionals as Certified Tobacco Treatment Specialists

National Registry and Master List of Certified Tobacco Treatment Specialists
www.umassmed.edu/tobacco/training/nat_registry.aspx

Texas A & M Health Science Center Baylor College of Dentistry, Dallas, Texas
Baylor Tobacco Treatment Services 214-828-8379
www.tambcd.edu

[a]The University of Medicine and Dentistry of New Jersey Tobacco Dependence Program
www.tobaccoclinic.org/
http://tobaccoprogram.org
http://tobaccoprogram.org/tobspeciatrain.htm

[a]The University of Massachusetts Medical School
http://umassmed.edu/tobacco/index.aspx

[a]The University of Mississippi Medical Center
http://act2quit.org
http://act2quit.org/treatment/
www.act2quit.org/education/certified-tobacco-treatment-specialist-.asp

[a]Florida State University College of Medicine Area Health Education Center (AHEC)
http://med.fsu.edu/index.cfm?page=ahec.tobaccoTreatment
http://med.fsu.edu/index.cfm?page=ahec.quitSmoking

[a]Mayo Clinic Nicotine Dependence Center Education Program, Rochester, Minn.
Tobacco Treatment Specialist Program (800) 344-5984
http://mayoclinic.org/stop-smoking/rsttreatment.html
http:/ndc.mayo.edu/mayo/research/ndc_education/tts_certification.cfm

Mayo Clinic, Scottsdale, Arizona
http://mayoclinic.org/stop-smoking/scttreatment.html

Carolinas Healthcare System 704-355-7808
http://www.carolinashealthcare.org

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[a]Facilities offering training for tobacco treatment specialists.

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BOX 15.3 Phone Apps for Smoking Cessation

Name	Cost
Quit Smoking-Cold Turkey	$0.99–4.99
Livestrong My Quit Coach-Dare to Quit Smoking	Free–$0.99
Quit Smoking	$4.99
Stop Smoking Forever	$7.99
Quitting Smoking	$2.99
Shocking Smoking Facts	Free
No Smoking-WellCall, Inc.	Free
The Joy of Quitting	$1.99
The Joy of Quitting Lite	Free
Smoke Track	Free
I Quit	Free
My Stop Buddy-Quit Smoking	$2.99
QuitGuide-MMG, Inc.-Tobacco Control Branch of National Cancer Institute	Free
Tobacco Tracker	Free
Tobacco Quitter App Bundle	$1.99
Cost of Smoking	$0.99
Smoking Horrors	$0.99
SmokErOut-The	$0.99
Quit Smoking Guide	$1.99
Quit For Life-Program, Free & Clear, Inc.	Free
10 Ways to Quit	$29.99
Help I Want to Give up Smoking	$3.99
Motivationizer-Quit Smoking	Free
A Guide to Quitting Smoking	$9.99
How to Quit Smoking Today	$9.99
How to Never Smoke Again by Alex Dollery	$7.99
No Smoking	Free
Q Smoking	$0.99
Quit Smoking Assistant	$0.99
Smoktivation:mymotivation	$0.99
Smoke Alarm-Your Friend	Free–$0.99
How To Quit Smoking	$0.99
No + Tobacco With Coaching	$0.99
Quit Advisor	Free
No Smoking Pro!	$0.99
Myintake	$0.99

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(2011a) suggest research into various populations who use these products as well as clinical interventions for the various stages of submucous fibrosis. Several stages have been suggested. Stage 1 produces general stomatitis; stage 2, fibrosis; and stage 3, premalignant leukoplakia-type lesions.

Oral submucous fibrosis (OSF) is a premalignant condition seen predominantly in Southeast Asia with the use of betel nut, areca nut, and tobacco products discussed above. The mucosa loses its elasticity, and dense fibrous bands can often be palpated. It is typically progressive, and some patients develop carcinoma as the disease progresses. Submucous fibrosis may even be observed in the young, who may have only used quid products for a short period (Nair et al., 2004). Figure 15.10C depicts a 54-year-old woman from India who has used betel quid from late adolescence and was diagnosed with OSF. The pigmentation and white striation in the buccal mucosa region are due to the extensive use of betel quid. Often noted as well are the wrinkled appearance, thickening of the mucosa, a marble-like appearance of white striations, and occasionally ulceration. Recent studies by Rao (2010) used alpha lipoic acid, an antioxidant, in conjunction with intralesional steroid injections (betamethasone) and hyaluronidase. Alpha lipoic acid is able to scavenge more wayward free radicals that other antioxidants. The study treated two groups of patients who were diagnosed with SMF with one group receiving the added ingredient of alpha lipoic acid over a 3-month period. The group receiving the added ingredient of alpha lipoic acid resulted in statistically significant improvements. Other studies have suggested that both lycopene and curcumin may have benefits of both antioxidant ability and anti-inflammatory capabilities. Studies suggest an anticarcinogenic ability of lycopene in oral cancer (Kumar, 2007).

Betel quid use is becoming more common in the United States, increasing the likelihood that clinicians will observe this type of tissue appearance in their practices. Also being introduced in the United States is the use of the sweet, flavored cigarettes called bidis. Other tobacco products once found only in other countries are now more common in the United States. Careful counseling regarding the potential danger of the use of the products is clearly indicated. Additionally, for those using the products, careful documentation and monitoring is necessary.

Congenital or Genetic Disorders

Congenital or genetic disorders are discussed thoroughly in Chapter 6. Chapter 23 presents the cutaneous pigmented-type lesions and the benign and malignant forms that may be part of the extraoral examination. However, some nevi may be perioral, affecting the lip area, and some are found intraorally. The patient may also, on occasion, have lip involvement that may affect the wet line of oral tissues.

NAME: Nevus (blue nevus)

Etiology: **Nevus** (pl., nevi) is commonly referred to as a mole and infrequently seen orally. It is also known as pigmented nevus, melanocytic nevus, and nevomelanocytic nevus. The nevus is classified as benign but may appear similar to the early stage of melanoma. There are several different forms of a nevus including, in order of their frequency, the **intramucosal nevus,** the **blue nevus,** the **compound nevus,** and the **junctional nevus.** The pigmented intraoral lesion is also sometimes referred to as mucosal nevomelanocytic nevus, or melanocytic nevi. There is a genetic predisposition to the nevus, and most adults have from 20 to 40 distinguishable nevi present on the observable external skin surfaces. A person who has more than 50 nevi on his or her body is considered high risk for skin cancer (see Clinical Protocol #10). The **blue nevus** is the second most common

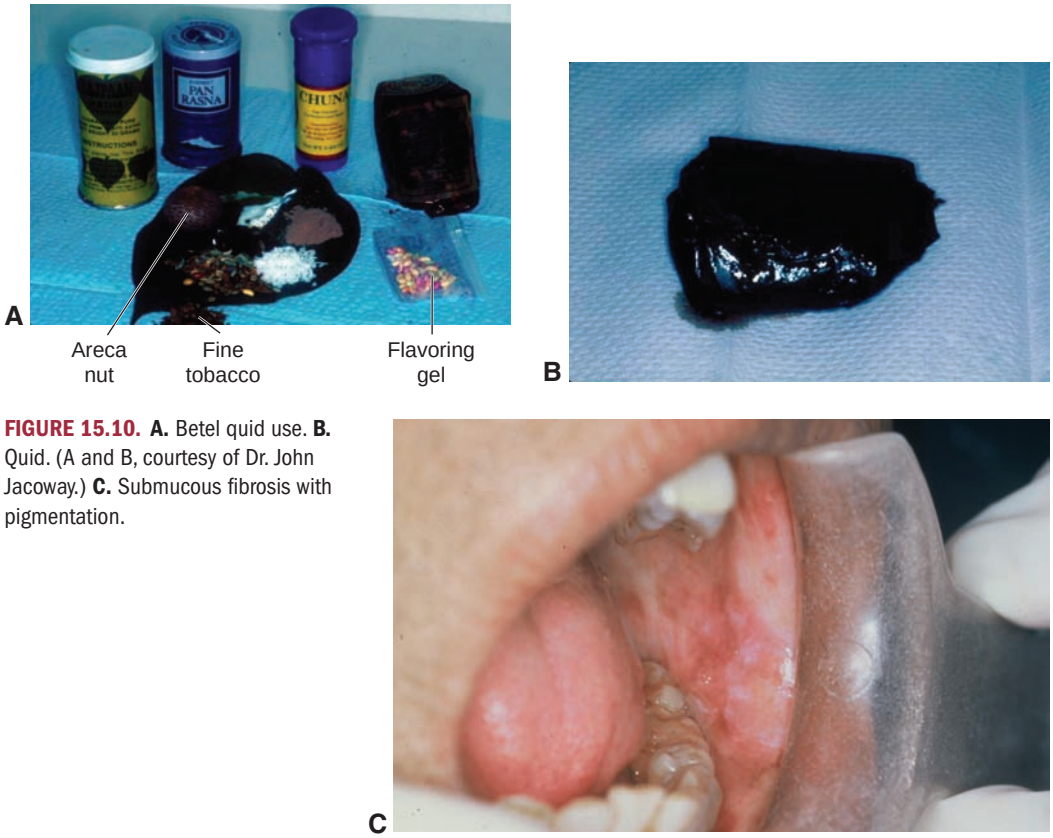


FIGURE 15.10. A. Betel quid use. **B.** Quid. (A and B, courtesy of Dr. John Jacoway.) **C.** Submucous fibrosis with pigmentation.

type of melanocytic nevus and accounts for approximately 16% of all oral nevi (Buchner et al., 2004). Blue nevi usually occur on the palate, followed by the buccal mucosa, and have been reported to become malignant in some instances.

Method of Transmission: Not applicable

Epidemiology: All age groups are affected with common moles, and many appear during childhood. However, individuals in the third and fourth decades are most often reported as seeking treatment for nevi, probably because they become aware of skin lesions in general at this time. There is no sex predilection. Approximately 20% are nonpigmented. The majority of nevi are located above the waist, with the head and neck affected most often. Most nevi are less than 6 mm in diameter. Whites are affected most often, followed by Asians and Blacks. The intramucosal nevus is rare but may occur, causing concern because of the similar appearance of a malignant melanoma.

Pathogenesis: The nevus occurs from nevus cells in the epithelium, the basement membrane, the connective tissue, or a combination of these. Nevi are believed to originate because of melanocyte migration from the neural crest to the epithelium and dermis; or additionally, from the proliferation of melanocytes.

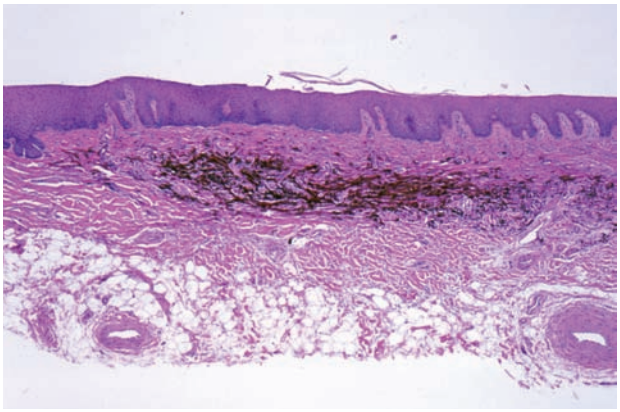
Extraoral Characteristics: The nevus may occur on any cutaneous surface. The extraoral nevus is discussed further in Chapter 23.

Perioral and Intraoral Characteristics: The intramucosal nevus is rare. Nevi are usually found in the palatal region and, to a lesser degree, in the buccal mucosa. Nevi may be seen clinically in shades of gray, brown, and blue. They are usually well circumscribed and slightly raised. Because of the slight possibility of malignant transformation, all intraoral nevi are removed surgically. This is not only because of the transformation possibility but because it would be impossible to clinically differentiate a pigmented nevus from a melanoma.

Distinguishing Characteristics: A distinguishing characteristic of the nevus is the pigmented color of the lesion when compared with normal mucosal skin tones. Additionally, any nevus lesion may be elevated and should be recorded in three-dimensional documentation, such as 2 × 2 × 3 mm.

Significant Microscopic Features: Nevi are classified according to the location of the nevus cells in relation to the basal cell membrane. For instance, a junctional nevus is found between the epithelium and the connective tissue. A compound nevus has nevus cells that have proliferated with groups of cells that drop off into the underlying dermis. Since cells are now not only in the basement membrane, but also in the underlying dermis, they are referred to as a compound nevus. The third classification is the **intradermal nevus** or **intramucosal nevus,** and the nests are found in the connective tissue. When the nevus is found in the oral tissue, it is referred to as an intramucosal nevus. Figure 15.11A shows a nevus in the palatal region. Figure 15.11B shows the histology of the intramucosal nevus. Note the increased pigmentation of the nevus cells within the tissue. Figure 15.11C depicts the blue nevus.

A


B

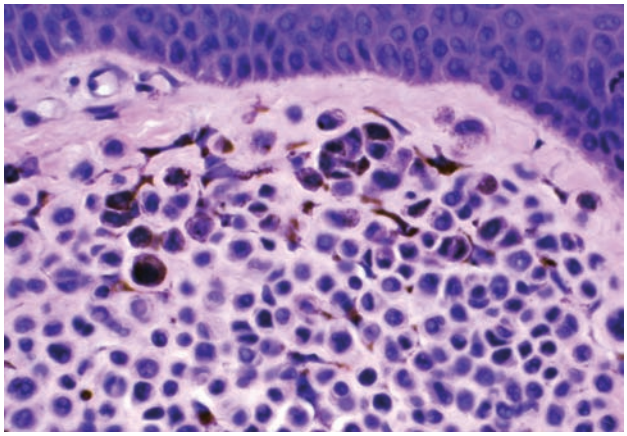

C

FIGURE 15.11. A. Palatal nevus. (Courtesy of Dr. Jeff Burkes.) **B.** Histology of an intramucosal nevus. (Courtesy of Dr. John Wright.) **C.** Histology of a blue nevus. (Courtesy of Dr. John Wright.)

Dental Implications: Although the cutaneous nevus is monitored and usually not removed unless suspicious, the intraoral nevus must be differentiated from a melanoma through removal and biopsy. Melanoma is highly malignant and must be treated rapidly and totally removed.

Differential Diagnosis: Considerations include:
1. Amalgam tattoos, Chapter 15
2. Melanoma, Chapter 15
3. Kaposi sarcoma, Chapter 22
4. Hemangioma, Chapter 13

Treatment and Prognosis: Biopsy is performed on the intraoral nevus, which is totally removed during the surgery. The area in question should be monitored, and any subsequent areas should be biopsied as well.

NAME: Oral melanotic macule (focal melanosis)

Etiology: A focal pigmented lesion that occurs on the lip or the intraoral tissues is referred to as an oral melanotic macule or labial melanotic macule.

Method of Transmission: Not applicable

Epidemiology: **Labial melanotic macules** (occurring on the lips) most often are seen in children and individuals in the 20- to 30-year-old age group. The intraoral lesions usually occur in patients older than 40. However, they may occur at any age and affect approximately 3% of the population, with the lip being the most common location. Focal melanosis is more commonly found in women.

Pathogenesis: The melanosis occurs on the vermilion border of the lip or the gingiva, because of postinflammatory or posttraumatic causes. Melanotic macules usually arise from three sources: an intraoral freckle, postinflammatory pigmentation, or disorders such as Addison disease, Peutz-Jeghers syndrome, or Laugier-Hunziker syndrome.

Extraoral Characteristics: The macules appear as single lesions that are pigmented, flat, and well delineated.

Perioral and Intraoral Characteristics: Melanotic macules that occur on the buccal mucosa are usually multiple. The macules are most often seen on the lip, followed by the palate and gingival and buccal mucosa. When occurring on the lip, the appearance is that of a freckle, known as an **ephelis.** Ephelides (pl.) tend to be less than 0.5 cm and are associated with sun exposure, in contrast to the focal melanotic macule, which is not associated with solar damage. Figure 15.12A depicts a melanotic macule on the lip of a female. Figure 15.12B shows a melanotic macule on the lip of a male.

Ephelides are usually found in fair-skinned individuals, are due to sunlight exposure, occur in childhood, and have a tendency to diminish with age. The ephelides may be indistinguishable from melanotic macules without viewing them under the microscope. Histologically, ephelides have fewer melanocytes but have more melanosomes, which are larger in

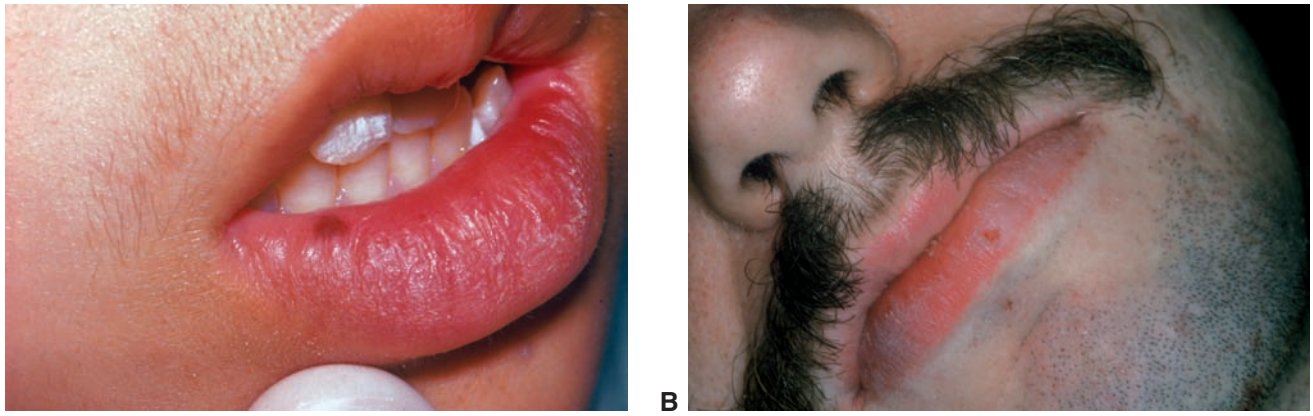


FIGURE 15.12. **A.** Macule. (Courtesy of Dr. Peter Jacobsen.) **B.** Melanotic macule. (Courtesy of Dr. E.J. Burkes.)

size. Using a sunscreen of 15 SPF will help to fade the ephelis. In contrast, **solar lentigines** are usually seen in older individuals, are much larger than ephelides, and tend to persist indefinitely even with sun protection (see Chapter 23). The macules are larger and appear more pigmented than ephelides. A good example is the backs of the hands of a fair individual who has been exposed to the sun over a period of time.

Distinguishing Characteristics: The melanotic macules are usually brown, deep blue/black, or black, and they are well-circumscribed with sharp, delineated borders.

Significant Microscopic Features: Melanin in the basal cell layer, lamina propria, or both are microscopic characteristics of a macule.

Dental Implications: When changes occur with these lesions, such as increased growth or shape, there could be a suspicion of a lesion that is characterized by early atypical melanocytes called **lentigo maligna.** These lesions exhibit atypical melanocytes in the epidermis with potential to invade the dermis layer. Changes in size or color, or border irregularity must be viewed with suspicion. These lesions are often seen on the faces of older individuals. The possibility of melanoma is always of concern with any lesion change, whether the macule is a freckle, melanotic macule, or a lentigo maligna. Synonyms for the melanotic macules are Hutchinson freckle and melanotic freckle.

Differential Diagnosis: The differentiation of focal melanosis and ephelis is a prime consideration, and the following disease states are part of the differential diagnosis:

1. Addison disease, Chapter 7
2. Peutz-Jeghers syndrome, Chapter 10
3. Laugier-Hunziker syndrome, Chapter 15
4. Melanoma, Chapter 15

Disease-Associated Melanosis

Certain diseases are known to have hyperpigmentation as a characteristic. The different types of disease-associated melanosis listed below are highly correlated with oral pigmentation and are of prime concern in a differential diagnosis:

1. Addison disease, Chapter 7
2. Peutz-Jeghers syndrome, Chapter 7
3. Lung diseases
4. Chronic lichen planus, Chapters 13 and 14
5. Polyostotic fibrous dysplasia, Chapter 10
6. Laugier-Hunziker syndrome, Chapter 15
7. Neurofibromatosis, Chapter 17
8. Albright syndrome, Chapter 10
9. Kaposi sarcoma, Chapter 23

Although all of the above-mentioned diseases are not discussed in detail here, they are mentioned in the general pathology section in relation to endocrine function and genetic disorders. Chapters 7 and 10 cover both endocrine and other diseases of concern in dentistry.

Treatment and Prognosis: The prognosis for the oral melanotic macule is excellent, and they are followed and monitored through documentation and photographs. No treatment is needed unless a biopsy is indicated because of changes or there is a question regarding the etiology of the macule.

NAME: Laugier-Hunziker syndrome (LHS, idiopathic lenticular mucocutaneous pigmentation)

Etiology: Some diseases and disorders have an unknown etiology with no history of a genetic or congenital history. One such disease, **Laugier-Hunziker syndrome,** has a distinct characteristic of pigmentation that mimics several of the pigmented lesions mentioned above. LHS is an acquired, benign, idiopathic, macular hyperpigmentation of the lips and oral mucosa, as well as other cutaneous areas, and often with nail pigmentation (Siponen and Salo, 2003). Although it is a benign condition, LHS may be confused with other pigmented diseases, and an incorrect diagnosis may occur. The patient may be treated for far more serious disease states.

Method of Transmission: Not applicable

Epidemiology: LHS was first described in 1970 with cases reported mostly in white populations. Women are affected more frequently than men, and the average mean age is reported to be 52 with a median age of 42 (Sachdeva et al., 2011).

Pathogenesis: LHS is thought to be linked to a functional alteration of the melanocytes that induce increased synthesis of melanosomes and their subsequent transport to the basal layer cells. The cause is unknown (Siponen and Salo, 2003). Pigmentation usually develops in early to middle adulthood (Sachdeva et al., 2011).

Extraoral Characteristics: Nail involvement occurs in approximately 50% of patients. Figure 15.13A depicts a woman diagnosed with LHS with mild nail pigmentation. Some nail pigmentation may present with thick wide bands of hyperpigmentation and appear as Hutchinson sign, a marker of subungual melanoma. Macules may range from 1 to 5 mm. on toes, fingers, lips and other cutaneous areas. Since these macules develop in midlife, the appearance can be very upsetting to the patient, and there may be a tendency by both patient and practitioner to fear the worst.

Perioral and Intraoral Characteristics: Dark brown pigmentation is most often seen on the buccal mucosa and lips. The hard and the soft palate may also be involved and, less frequently, the gingiva, the floor of the mouth, and the tongue. Figure 15.13B shows the same woman with pigmentation throughout the lip area. Figure 15.13C depicts the woman with pigmentation in the buccal mucosa.

Distinguishing Characteristics: The nail pigmentation is characteristic, containing bands or streaks of pigmentation. Racial pigmentation occurring orally or in the nails is not usually seen in whites.

Significant Microscopic Features: Microscopically, basilar melanosis with increased numbers of melanophages in the lamina propria is normally present.

Dental Implications: The pigmentation may occur suddenly, and the patient may be apprehensive about the cause. Because the syndrome is often not recognized as LHS, the patient may face extensive testing, and the symptoms may be confused with many other disease states. Proper recognition is crucial.

Differential Diagnosis: Diseases that have pigmentation as a characteristic should be considered, such as

1. Addison disease, Chapter 7
2. Peutz-Jeghers syndrome, Chapter 10
3. Smoking-associated melanosis, Chapter 15
4. Medications that produce pigmentation, Chapter 15
5. Physiologic pigmentation, Chapter 15
6. Heavy metal pigmentation, Chapter 15
7. Postinflammatory disorders, Chapter 15

Peutz-Jeghers disease involves gastrointestinal polyps, pigmentation of the hands and feet, gastrointestinal carcinoma, and genital and mammary tumors; thus, differentiation is crucial to seeking treatment for patients with Peutz-Jeghers disease. Because of the pigmentation in both disorders, diagnostic differentiation is often a problem. Chapter 10, "Respiratory, Gastrointestinal, Neurologic, and Skeletal Disorders," includes a full description of this type of pigmentation.

Treatment and Prognosis: The syndrome is benign, but its importance is relevant to being included in the differential diagnoses of pigmentary disorders of the oral mucosa, since it may be confused with more serious diseases such as Addison disease (Chapter 7), melanoma (Chapters 5, 15, and 23) and Peutz-Jeghers disease. The correct diagnosis ensures that unnecessary tests, patient anxiety, and unneeded treatments are avoided. When cosmetic concerns are voiced, laser surgery is often performed. The patient should be counseled to wear sun protective clothing and sunscreen daily.

Neoplasms

Neoplasms associated with pigmented lesions are rare and very aggressive, with an unpredictable pattern. The most common pigmented neoplasm in the oral cavity is the melanoma. Skin or external lesions are more common, but any pigmented lesion must be assessed to rule out the possibility of a malignancy. Oral melanoma is discussed next in this chapter and is also discussed as a cutaneous melanoma lesion fully in Chapter 5 and in Chapter 23 on skin diseases.

NAME: Oral melanoma

Etiology: Malignant oral melanomas of the head and neck region are rare and account for 0.2 to 0.5% of all melanomas in the United States (Regezi et al., 2003; Meleti et al., 2007). The cutaneous melanoma rate is more pronounced in certain areas of the world where the sun is more intense. Oral melanoma occurs in the oral tissues that are not exposed to the sun, and the etiology is very different for oral melanomas and not as clearly understood. Although the etiology of the oral melanoma is unknown, tobacco use (Meleti, 2006), chronic irritation, formaldehyde exposure, familial history, and cytogenetic defects may play some role in its

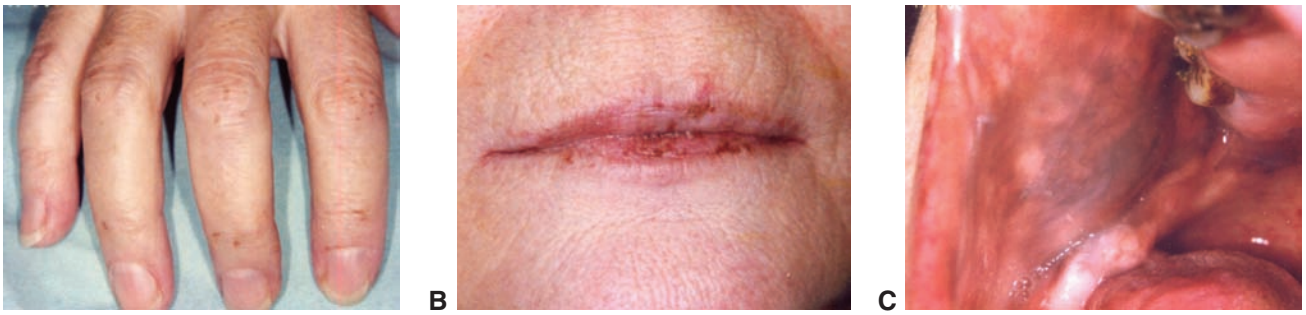


FIGURE 15.13. A–C. Laugier-Hunziker syndrome. (Courtesy of Dr. Maria Siponen.)

development. A pigmented area, usually in the palate or the maxillary gingiva, precedes most oral melanomas.

Method of Transmission: Not applicable

Epidemiology: Oral melanoma accounts for approximately 0.02 to 8% of all melanomas in Europe and the United States and 5% of all oral malignancies (Gu et al., 2003). Melanomas usually occur in the fourth decade or later, with an average age of 56 (Barker et al., 1997), and the occurrence is extremely rare in children and young adults. Oral melanomas occur more often in males. Recent retrospective studies by Wang et al. (2011) reported on a group of 61 patients diagnosed with oral melanoma. The researchers reported a 2.1:1 ratio of male to female patients and a mean age of 54.1. The rate of cutaneous melanomas among the young has dramatically increased in the past few years, and this continuing increase is discussed further in Chapter 23 on skin diseases. Ethnicity is a factor associated with the development of melanomas in general. For example, more melanomas are found in Japan (Takagi et al., 1974) and Uganda, with Native Americans and Latinos exhibiting higher rates in the United Sates. Tomicic and Wanebo (2003) suggest that the rarity of the melanoma makes progression in treatment difficult and advances slow. Researchers suggest that of those who were born in the year 2000, 1 in 75 persons will develop cutaneous melanoma in their lifetime, compared with only 4 in 10 million persons who will be diagnosed with oral melanoma. Oral melanomas are preceded by an area of melanosis 30 to 50% of the time (Kahn et al., 2005). Retrospective studies by Kerr et al. (2011b) reported a high rate of sinonasal tract melanomas with local recurrences of 82% and distant metastasis of 92%; 47% were pigmented and 93% were ulcerated.

Pathogenesis: Sunlight, the environment, and even genetic factors appear to influence the development and progression of melanomas. Several subtypes of melanomas exist: the in situ melanoma and the invasive-type melanoma. The in situ type may exist in a localized growth phase for months or years before becoming a more invasive form of melanoma with vertical growth patterns. The absence of pain in many cases is a factor in the failure of the patient to seek treatment, which results in not diagnosing a lesion until the later stages, which are associated with a poorer prognosis.

Extraoral Characteristics: The cutaneous lesions related to melanoma are discussed in Chapters 5 and 23.

Perioral and Intraoral Characteristics: The most commonly affected sites are the hard palate and maxillary gingiva. The melanoma is usually a brown, red, black, and even black-bluish color and may be slightly raised, with irregular borders. The lesions may have a rapid growth pattern, with a deep invasive nature. Melanomas may appear exophytic or ulcerative, and the colors may be mixed, depending upon the stage of the neoplasm. Asymmetry and irregular borders are key signs related to melanomas. Enlarging masses, whether pigmented or amelanotic (those that are more flesh colored), should have a biopsy performed to determine the diagnosis. Figure 15.14A depicts a malignant melanoma of the gingiva. Figure 15.14B depicts a malignant melanoma

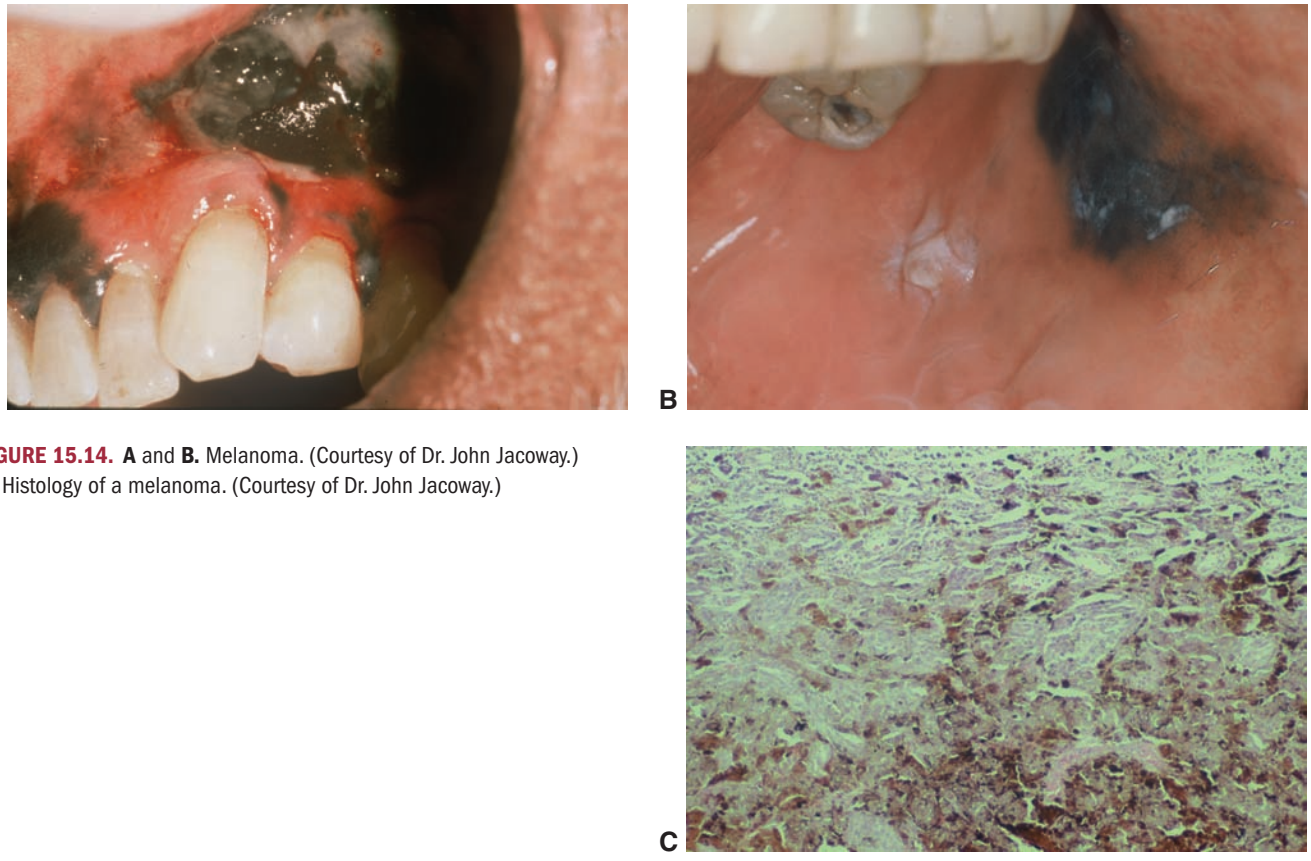


FIGURE 15.14. **A** and **B.** Melanoma. (Courtesy of Dr. John Jacoway.) **C.** Histology of a melanoma. (Courtesy of Dr. John Jacoway.)

in the posterior retromolar area and buccal mucosa area. Figure 15.14C depicts the histologic specimen demonstrating malignant melanocytes.

Although this discussion concerns pigmented lesions, in some cases melanomas may be light-colored as well, blending into the surrounding tissue, and may be referred to as an **amelanotic melanoma.** Some pigmentation may also be interspersed in the lesions and may precede the actual clinical manifestation of the amelanotic melanoma.

Distinguishing Characteristics: The intraoral melanoma may appear as a dark blue to black pigmented area with irregular borders increasing as the lesion continues to expand.

Significant Microscopic Features: The pathology shows malignant proliferation of melanocytes. Figure 15.14C shows the histology of the lesions, displaying a radical growth phase. The tumor is spreading laterally through the epithelium. The rounded collections of cells are the malignant melanocytes.

Dental Implications: The intraoral melanoma is a deadly lesion that should be recognized and removed in its earliest stage. Early melanomas may be confused with other pigmented lesions such as the blue nevus discussed previously or an amalgam tattoo, and the poor prognosis has been attributed to the fact that there is often a delay in recognizing the lesion as a melanoma. Additionally, there is confusion with other lesions that are benign, causing a delay in treatment. Since pain is not a feature of the lesion, the patient may present at much later stages.

Differential Diagnosis: Several pigmented lesions should be evaluated when a diagnosis is being considered, including:

1. Intramucosal nevus or blue nevus, Chapter 15
2. Amalgam tattoo, Chapter 15
3. Kaposi sarcoma, Chapter 22
4. Physiologic pigmentation, Chapter 15
5. Melanotic macule, Chapter 15

Treatment and Prognosis: The rich vascular network found in the oral tissues makes the oral melanoma very aggressive with a much poorer prognosis than melanomas found elsewhere on the body; therefore, any pigmented lesion in the oral cavity should be viewed with suspicion. The growth rate and the tendency of oral melanomas to metastasize remain high. Therefore, early detection and treatment are of extreme importance. Excision of the oral melanoma is the course of action, with wide surgical margins because recurrence is common. Clear margins are critical in this type of neoplasm. Chemotherapy and radiation for head and neck cancers may be used as well, depending upon the size, location, and progressive nature of the lesion. Promising techniques are being used in some forms of cancer with **biologic therapy** that stimulates or restores the ability of the immune system to fight cancer, infections, and other disease states.

Oral melanomas are associated with a poor prognosis because of the tendency to metastasize to other organs and tissues. Five-year survival rates vary, with reports from 4.5 to 29%. Meleti et al. (2007) suggest that there is a 5-year survival rate of approximately 15%.

SUMMARY

- Physiologic pigmentation is a variant of normal. Physiologic pigmentation is found in varying degrees in all ethnic groups.
- Oral pigmentation is essentially due to (1) the number of melanocytes, (2) the amount of melanin produced, or (3) the incorporation of a foreign substance introduced into the oral and perioral tissues.
- Amalgam tattoos are the result of amalgam particles within the oral tissues that produce a gray, blue, or black hue. Amalgam fragments may be seen on radiographs, which aids in the definitive diagnosis of an amalgam tattoo.
- A blue-gray pigmented area may be found from intentional tattooing performed in some cultures by using soot and metal dust, usually performed during childhood.
- Pigmentation may occur in conjunction with some titanium implants.
- Minocycline staining, also referred to as black bone staining, results from ingestion of minocycline, which is a semisynthetic derivative of tetracycline. This medication is often used in the treatment of acne in adolescents and young adults.
- Tobacco-associated melanosis results from the long-term use of tobacco products. A soft brown pigmentation is produced, usually in the palate and buccal mucosa.
- Submucous fibrosis is caused by betel quid and tobacco that is used in some cultures, and it is considered a premalignant condition.
- Heavy metal pigmentation is caused by the ingestion of heavy metals such as lead, bismuth, arsenic, and mercury. The exposure is usually occupational and occurs commonly through vapors. The disposition of lead in the tissue is referred to as "lead-line staining" and appears as a line at the gingival margin of the teeth.
- A nevus is commonly referred to as a mole. There are several classifications of the nevus: junctional, compound, intramucosal, and the blue nevus.
- The nevus found in oral tissues is called the intramucosal nevus.
- Oral melanotic macules or focal melanosis (freckles) are described as benign pigmented lesions and are usually found on the lips and the palate regions. The pigmentation may be associated with inflammation or sometimes disease states such as Peutz-Jeghers syndrome or Addison disease.
- Certain disease states are associated with pigmented lesions and pigmented perioral tissue: Addison disease, McCune-Albright disease, Peutz-Jeghers disease, and Laugier-Hunziker syndrome.

- The melanoma appears as a painless, usually fast-growing, blue-black lesion with a predilection for the gingiva. The amelanotic melanoma appears as more flesh colored, although some prior pigmented area is usually reported.
- Any pigmented lesion should be investigated and have a cause established.
- Any pigmented area of tissue should be monitored, if not biopsied and removed.

CHAPTER REVIEW

Case Study 15.1

The patient in Figure 15.15A is a new patient in your practice.

As you begin your extraoral exam, you notice the area on her upper lip. Using the images presented (Fig. 15.15A and B), determine whether the raised area on her lip is of concern. Consider the following:

1. What questions would you want to ask her?
2. What characteristics of the lesion might make you concerned or what characteristics might make you feel this is likely benign in nature?
3. What does the histology of the lesion denote?
4. What other conditions should be considered in a differential diagnosis?
5. Are there any tests or procedures that your office would recommend?

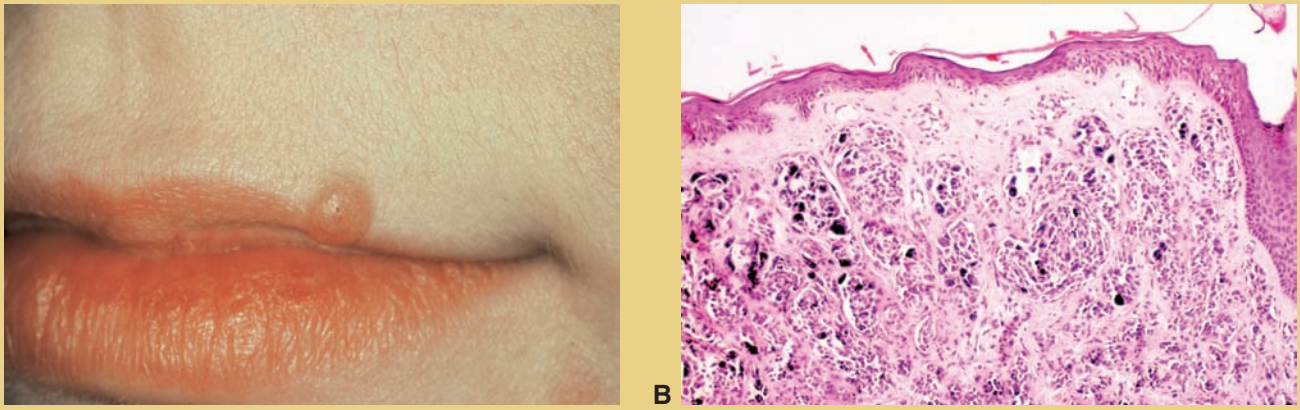


FIGURE 15.15. A. (Courtesy of Dr. Nancy W. Burkhart.) **B.** Histology.

For answers and additional review activities, log in to **thePoint.lww.com**

Case Study 15.2

This patient is a 16-year-old male seeking dental hygiene care. It has been several years since his last appointment. His parents are concerned because he has had a fever and sore throat for several days and now he has blisters on his lip. He has been taking antibiotics (left over from a previous strep infection), but they have not had any effect on his symptoms. The parents are looking for answers, and they are very concerned about their son. Given the three images of this patient (Fig. 15.16A–C), please evaluate the following questions.

1. What would be your best estimation regarding the cause of these vesicles on his lip?
2. How would you describe the tongue? What are the white plaques you observe?
3. How would you describe the tissue around the third molar region in #17 and #32 areas?
4. In which of the following categories would you place the signs/symptoms of this patient? This is based on what you see as the visual characteristics of the patient.

Additionally, what other diseases that you know of could be listed in each category?

a. An immunodeficiency
b. Hematologic malignancy
c. Viral infection
d. A systemic condition
e. Immunosuppressive therapy

A

B

C

FIGURE 15.16. A–C (Courtesy of Dr. U. Sharma and Dr. S. Bhalla.)

For answers and additional review activities, log in to **thePoint.lww.com**

Critical Thinking Activities

Figure 15.17 depicts a heavily pigmented area of the palate. The patient is a 40-year-old female who is a new patient. Pigmented areas are also found on the patient's fingers, lips, and buccal mucosa.

1. What questions would you ask the patient during your examination of the oral tissues?
2. What facts would you expect to see on the health history that would help you make a determination or perhaps rule out a possible cause?
3. What external lesions would concern you or make you curious?

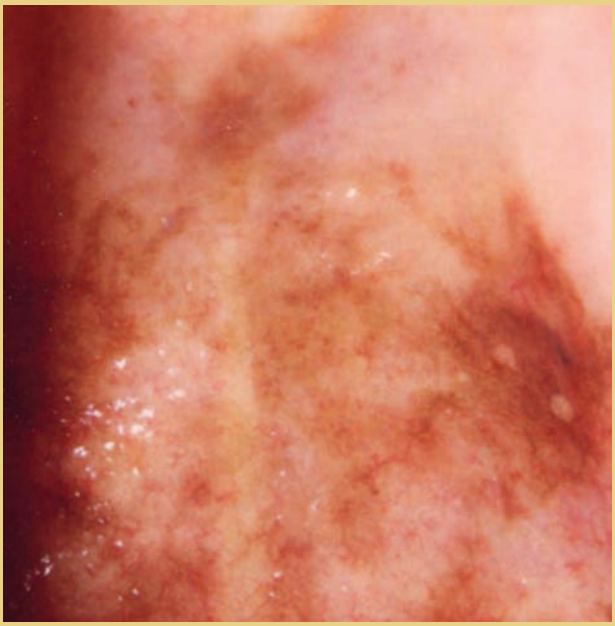


FIGURE 15.17. (Courtesy of Dr. Maria Siponen.)

Portfolio Possibilities

- Develop a set of standards for your office on intraoral photographs to monitor lesions. If you do not have an intraoral photography system in place, discuss the benefits of having such a system with your peers and other staff members. Perhaps a short document on the benefits to both the patients and the staff for long-term health and for legal purposes could be a marketing tool for your office. Since many offices do not have a photography protocol for the office, this could be a major asset for your office.
- Research and make a list of the types of medications, diseases, and chemicals that may produce pigmented lesions. Use this chapter and other resources.
- Determine local dermatologists in your neighboring area who would like to have referrals from your office when a patient is found to need further evaluation. Your office may provide literature on common skin lesions and ways that they can protect themselves and family members from sun damage (see Clinical Protocol #10).

Media Menu

Web Sites

The following Web sites are listed as possible resources for this chapter. Additional organizations and phone apps regarding smoking cessation are listed in Boxes 15.2 and 15.3.

National Institute of Arthritis and Musculoskeletal and Skin Diseases
www.niams.nih.gov

American Dental Hygiene Association—general oral health information
http://www.adha.org/oralhealth/index.html

American Cancer Society—Information and resources for cancer
http://www.cancer.org/

World Health Organization
http://www.who.int/en/

Study Tools

Take advantage of additional online resources to help you study and ace your exams!

- Answers to case studies in the book
- Additional case studies and answers
- Interactive quiz bank with answer feedback
- Fully searchable e-book for quick lookup and studying on-the-go
- Expanded Media Menu with direct links to related Web sites and multimedia resources
- Supplemental references

thePoint Online resources and links are available at http://thepoint.lww.com/DeLong2e.

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Chapter 15 **LESION/CONDITION SUMMARY TABLE**

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Physiologic Pigmentation	Each individual produces a varying number of melanocytes. Increased pigmentation may occur due to hormonal factors and ethnicity.	Individual tendency to produce more or less melanin. The sun damages the skin causing the production of more melanin as a protective measure in environmental pigmentation (tanning).	Darker pigmented areas may be seen both extraoral and intraorally. The colors may range from light brown to blue/black.	Increase in melanin within the basal keratinocytes. Some melanin is also found in the connective tissue due to dendritic transfer of the melanocyte processes.	Confirmation is the main objective. Other disease states such as Addison disease, Peutz-Jeghers syndrome, and melanoma produce pigmented areas.	Cosmetic concerns are issues for patients when pigmented areas can be seen while speaking or if they appear on the lip tissues.
Traumatic or Inflammatory Lesions	Trauma or irritation to the tissue Chemicals, medications, thermal changes	The tissue is imbedded with foreign objects. Disease states that cause inflammation, smoking, spit tobacco, and ethnic tattooing.	Tissues appear brown or dark in color.	Tissue may contain varying particles that pertain to the etiology of the pigmentation	Removal of the offending objects and reduction of inflammation.	A definitive diagnosis is crucial to rule out possible pathology. Assurance to the patient that the area of concern is not serious is important. Reduction of inflammation anywhere in the body is needed and key to good overall health.
Amalgam Tattoo Focal Argyrosis	Amalgam particles imbedded within the tissues	Amalgam fragments within the tissues cause dark pigmentation of oral structures.	Dark pigmentation	Radiopaque particles that may appear solid or dispersed.	No treatment is needed.	Confirmation of amalgam particles is needed to rule out more serious disease states such as melanoma.
Titanium Tattoo	Particles of titanium-ions	May occur in initial preparation of the crown or possibly from leaching of ions from device.	Blue to gray diffuse pigmentation	Diffuse opacity. Particles can be detected microscopically.	No treatment unless the implant is failing, but other problems should be addressed such as peri-implant disease states.	Routine cleanings and follow-up evaluations of all implants would be crucial in overall good health.
Heavy Metal Pigmentation: Argyria, Lead and Bismuth	Exposure to various types of heavy metals	Metals may be ingested or inhaled, or exposure may occur through prolonged cutaneous contact.	Dark staining of tissues, bones, and teeth.	Some evidence exists in tissue that can be examined microscopically and confirmed to have metal properties.	Identification of the offending products and discontinuing them	The clinician must rule out other possible causes. Blood work and evaluation is often needed with tissue analysis.
Medication-Associated Pigmentation	AZT, mincocycline, tetracycline, oral contraceptives, hormone replacement therapy, tobacco, antimalarials, antitumor medications all contribute to oral pigmentation	Use of these medications affect the tissues and pigment various structures of the oral cavity.	Darker colored tissues may be evident and some areas such as the tongue are affected by discoloration of the papillae.	NA	Assessment of the tissues and a careful health history will assist in determining which medication may be causing the pigmentation that is observed.	Discontinuing the medication is the optimal choice or replacement with another brand that may not cause pigmentation. Monitoring any pigmentation is crucial.
Smoking-Associated Melanosis and Betel Quid Use	Tobacco-related pigmentation Chemicals and/or heat are factors in cigarette smoking, betel quid use, and spit tobacco.	Stimulation of melanocytes. Melanocytes function as a defense mechanism. With betel quid use, the highly pigmented betel nut causes deep staining.	Pigmentation of the tissues occurs and elongation of the papillae may occur. Betel quid use results in submucous fibrosis and is considered premalignant. Deep fibrotic bands cause constriction and tissue changes.	Increases in melanin are evident in basal keratinocytes. The appearance is similar to those of physiological pigmentation. The microscopic component of SMF consists of dense white bands and fibrotic tissues causing constriction. There is a tightening affect that prohibits mouth closure.	Oral cancer is increased with tobacco use and increases further when coupled with alcohol use. Betel quid products produce more of a red/brown pigmentation. Cultural elements are associated with the quid use as well.	Patients should be counseled on tobacco cessation; careful follow up of all tissues is crucial. Motivational interviewing is important here as well. Even though the patient may cease use, the tissues may be previously damaged with any earlier tobacco use.

continues

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Nevus	Nevi are believed to originate because of melanocyte migration from the neural crest to the epithelium and dermis.	Due to proliferation of melanocytes. Forms include intramucosal nevus (in oral tissue), blue nevus, compound nevus, and junctional nevus.	May appear flesh colored or dark blue, gray, or brown. In the case of the blue nevus the color is black/blue. The nevus is also found in the cutaneous regions.	The location is important in correct classification. Junctional nevus is between the epithelium and the connective tissue. A compound nevus has proliferation of nevus cells both in the dermis and basement membrane. Intradermal nevus nests are in the connective tissue. The term intramucosal nevus is used when found in oral tissues.	Intraoral nevus must be differentiated from the melanoma. Therefore, they are surgically removed and examined through biopsy.	Removal usually solves any question of malignancy. Monitoring of any lesion removed is optimal treatment.
Oral Melanotic Macule (focal melanosis) or Labial Melanotic Macule	Pigmented macule that occurs on the lip or the intraoral tissues. Affects 3% of the population, usually in the 20- to 40-year-old age group.	May occur on the vermillion border of the lip due to trauma or postinflammatory reasons. They usually arise from 3 sources: an intraoral freckle, postinflammatory pigmentation, or disease states such as Addison disease, Peutz-Jeghers syndrome, or Laugier-Hunziker syndrome.	Usually multiple lesionis occur on the buccal mucosa. Usual locations are the lip, palate, and gingival/ buccal mucosa. When on lip the appearance is that of a freckle (ephelis). Found in fair-skinned individuals, due to sunlight exposure, and are indistinguishable from the melanotic macule except under the microscope. Solar lentigos are usually seen in older individuals.	Melanin in the basal cell layer and lamina propria are both microscopic characteristics of a macule.	When changes occur, suspicion arises that there may be atypical melanocytes. Also called lentigo maligna.	Other diseases should be considered when pigmentation occurs such as: Addison disease, Peutz-Jeghers syndrome, lung disease, chronic lichen planus, Laugier-Hunziker syndrome, and others.
Laugier-Hunziker Syndrome	Etiology unknown	Thought to be a functional alteration of the melanocytes that induce increased synthesis of melanosomes and their transport to the basal layer cells	Pigmented macules from 1-5mm occurring on cutaneous and oral areas. Appear at mean age of 52.	Microscopically basilar melanosis with increased numbers of melanophages in the lamina propria	Pigmentation may occur suddenly and the patient may be apprehensive. Extensive testing may occur to rule out other disease states.	Laugier-Hunziker disease only requires a proper diagnosis and no treatment is needed for the disease. Laser surgery may be needed to correct any cosmetic concerns and proper sun-screen protection is crucial.
Oral Melanoma	Unknown, but environmental factors are noted: sunlight, formaldehyde, irritation, cytogenetic defects	Several subtypes exist: in-situ and invasive. Genetic factors may play a role and some melanomas go undiagnosed for months.	The hard palate and maxillary gingiva are prime areas. The melanoma may be black, blue or gray, or some may be amelanotic or present with a light brown to red color. Asymmetry and irregular borders are key signs.	Malignant proliferation of melanocytes	Failure to diagnose and remove a melanoma is the largest contributing factor in late stage treatment.	The prognosis is poor in most cases. Early treatment is needed to detect in an early stage of development. Rapid spread to distant organs is found in most cases.

CHAPTER 16

Raised Lesions with a Rough or Papillary Surface

KEY TERMS

Autoinoculation
HPV, low risk
HPV, high risk
Keratinization
Keratinocyte
Mitosoid figures
Parakeratotic
Reservoir

LEARNING OUTCOMES

1. Define and use the key terms listed in this chapter.
2. Discuss the characteristics of the human papillomaviruses (HPVs) and differentiate between the high-risk and low-risk types.
3. Describe the etiology, method of transmission, and pathogenesis of the lesions associated with HPV.
4. List the characteristics of the lesions caused by HPV and discuss their dental implications.
5. Describe the etiology, clinical characteristics, and dental implications associated with papillary hyperplasia.
6. Describe how papillary hyperplasia is usually treated.
7. Distinguish between papillary hyperplasia and papillary lesions caused by HPV.
8. Compare and contrast squamous cell carcinoma and keratoacanthoma.
9. Discuss the relationship between squamous cell carcinoma and verrucous carcinoma.
10. Identify the role of the dental hygienist in preventing cervical cancer.

CHAPTER OUTLINE

Infections
- Oral squamous papilloma
- Verruca Vulgaris
- Condyloma acuminatum
- Focal epithelial hyperplasia

Inflammatory or Reactive Lesions with a Papillary Configuration
- Papillary hyperplasia

Premalignat/Malignant Lesions Associated with a Rough or Papillary Surface
- Keratoacanthoma
- Verrucous carcinoma

RELATED CLINICAL PROTOCOLS

#14 Postoperative Instructions for Oral Surgery Patients
#15 Office Protocol for Identifying Suspected Family Violence
#18 Supplements for Oral/Systemic Health
#20 Oral Health Care Management for the Patient with HIV/AIDS
#24 Tobacco Cessation
#25 How to Utilize Nutrition Counseling in Practice
#27 Motivational Interviewing for Behavior Change

Raised lesions with a rough or papillary surface comprise a distinct group of oral mucosal masses that represent epithelial abnormalities. Among these are diverse malignancies, contagious infections (including viral proliferations associated with a large number of human papillomaviruses [HPVs]), sexually transmitted diseases (STDs), and reactive or inflammatory lesions. Since the most significant epithelial abnormality in the oral cavity is squamous cell carcinoma (SCC), all rough or papillary raised lesions should be managed as though they potentially could be SCCs. The goal of this chapter is to provide sufficient information to help the dental hygienist identify the clinical characteristics of these lesions and collaborate with other dental professionals to make appropriate recommendations for diagnostic and follow-up procedures.

Infections

The primary etiologic agent associated with lesions exhibiting a rough or papillary surface is the HPV. There are more than 140 different types and subtypes of HPV (Rubin and Strayer, 2012). One-third of HPV infections cause genital tract lesions. The median time from infection to the first detection of HPV is 3 months (Rubin and Strayer, 2012) and as many as two-thirds of women graduating from college have genital HPV infections. Some of these specific types are listed in Tables 16.1 and 16.2 along with the disorders with which they are associated. HPVs are members of the Papovaviridae family of viruses that produce epithelial tumors of the skin and/or mucous membranes. They are double-stranded DNA viruses that do not have an envelope surrounding them. They only affect humans, and humans are their only **reservoir** (substance or living host within which an organism can multiply and develop). Some HPVs have been associated with benign lesions and are identified as **low-risk types**. These viruses normally inject their DNA into the nucleus of the host's cells, where it exists within the nucleus as a separate entity. Others, designated **high-risk types**, have been associated with carcinomas and infect the host's cells in a different manner (Gillison, 2007). The viral DNA of high-risk types is integrated into the host's DNA, which results in malignant transformation of the host cell. Most HPV infections are benign lesions of squamous epithelium and include warts, laryngeal papillomas, and condylomata acuminata. Cancer of the uterine cervix has been associated with HPV-16 and HPV-18. Head and neck cancers including those of the tonsillar region have been associated with HPV-16 in approximately 25% of cases. Data indicate that HPV-positive status is correlated with a higher survival rate in patients diagnosed with oropharyngeal cancer (Ang et al., 2010; Gillison et al., 2008) when compared with HPV-negative patients. A paper published in 1986 by Depue called attention to the rise in the under 30-year-old age group who were diagnosed with cancer of the tongue. Subsequent reports and data supported the fact that HPV

TABLE 16.1 Epithelial Disease and Associated Human Papillomavirus Types

Disease	Human Papillomavirus Types[a]
Verruca vulgaris (common wart)	1, 2, 4, 26, 27, 40, 41
Focal epithelial hyperplasia	13, 32
Condyloma acuminatum	6, 11, 16, 18
Squamous papilloma	2, 6, 11, 57
Verrucous carcinoma	2, 6, 11, 16, 18
Keratoacanthoma	Possible 9, 11, 13, 16, 18, 24, 25, 33, 37, 57

[a]HPV types listed are the most common ones associated with the lesions; others are possible.

TABLE 16.2 Human Papillomavirus Risk Types

Risk Type	Human Papillomavirus Types
The high-risk types of the papillomavirus have been linked with cancers in both men and women.	HPV 16, 18, 31, 35, 39, 45, 51, 52, 58
The low-risk types cause cervical changes, genital warts, and respiratory papillomas. 100 reported types, 60 HPV types cause warts on the skin surfaces.	HPV 2, 6, 11, 13, 32, 57

was highly linked to this increase in oropharyngeal cancer patients who never smoked or never drank. Recent studies and reviews suggest that the role of HPV as a sole etiologic agent needs further evaluation (Kumaraswamy & Vidhya, 2011). Clinically, lesions associated with the HPV are exophytic, with a surface appearance that is cauliflower-like. As is the case with all infectious viruses, HPVs are transmissible, but their degree of infectivity varies from type to type. Benign lesions associated with HPV are discussed in this section.

NAME: Oral squamous papilloma

Etiology: HPVs 2, 6, 11, and 57 (all low-risk types) have been associated with benign oral squamous papillomas (Regezi et al., 2003).

Method of Transmission: HPV is transmitted by direct contact between the virus and nonintact mucosa. They have very low infectivity. The virus can also be spread by **autoinoculation** (transfer from one site to another on the same person).

Epidemiology: There are no prevalence data for the oral lesions alone; however, 7 to 10% of the population has some form of cutaneous or mucosal HPV-related lesion (Gearhart et al., 2006). Any age can be affected. There is equal distribution between the genders for oral and cutaneous lesions. Individuals who are immunosuppressed have a much higher risk of developing these lesions than those who do not have a compromised immune system. However, a higher number of females are infected with anogenital HPV than males (Gearhart et al., 2006). See Application 16.1 for information about HPV and cervical cancer.

Pathogenesis: Lesions associated with this virus are believed to arise from the proliferation of infected basal **keratinocytes** (living precursors to the dead keratin-filled cells of the stratum corneum on the outermost layer of the skin) (Gearhart et al., 2006).

APPLICATION 16.1

Human Papillomavirus and Cervical Cancer

In 2012, the most recent year numbers are available, 12,170 women in the United States were diagnosed with cervical cancer. In addition, 4,290 American women died from cervical cancer in 2011 (ACS, 2012). Cervical cancer was one of the major causes of cancer deaths in women in the United States before the Pap test became available in 1955. From 1955 to 1992, there was a 74% drop in the rate of cervical cancer deaths because of early detection (ACS, 2006). Recently, researchers have made dramatic advances in understanding the cause of, and in finding potential preventive strategies for, cervical cancer.

The most important risk factor for cervical cancer has been found to be infection with a human papillomavirus (HPV). The HPVs that are associated with most cervical cancers are the high-risk types HPV-16 and -18. Over 140 types of HPV are known to exist with more than 40 that may infect the genital area. HPV is sexually transmitted by skin-to-skin contact during vaginal and anal intercourse and by genital–oral contact. Using condoms and otherwise practicing "safe sex" have not been shown to be an effective preventive measure for HPV transmission because it is transmitted by skin-to-skin contact in addition to mucosal contact. Most women who are infected by the virus are never aware of their infection, and their immune system is able to eliminate it over a period of time. In some women, the virus stays in the cells. A small percentage of the women who retain the virus will develop cervical cancer. It is not known why some women with the virus develop cervical cancer while others do not, but researchers have identified several additional risk factors that, coupled with HPV infection, may increase the risk of developing cervical cancer. These include the following:

- Smoking and alcohol use
- HIV infection
- Coinfection with *Chlamydia*
- Diet (being overweight, diet low in fruits and vegetables)
- Long-term oral contraceptive use (5+ years)
- Multiple full-term pregnancies
- Family history of cervical cancer

The CDC estimates that 20 million people are currently infected with HPV, including about 75% of the reproductive age population. The CDC also expects up to 5.5 million new infections each year (CDC, 2011). The numbers are staggering, but new vaccines have been developed that have been shown to be 100% effective in preventing initial infection with HPV-16 and -18 (high-risk types that cause 70% of cervical cancers) and 99% effective in preventing infection with HPV-6 and -11 (low-risk types that cause 90% of genital warts). The Advisory Committee on Immunization Practices (ACIP, 2011) has approved two HPV vaccines that are licensed in the United States: a bivalent vaccine (Cervarix) containing HPV types 16 and 18 and a quadrivalent vaccine (HPV-4; Gardasil, Merck & Co. Inc.) containing HPV types 6, 11, 16, and 18. The vaccine, called Gardasil, has been approved for use in young women and men (October, 2009) to prevent infection with these viruses. The HPV-4 vaccine is effective in preventing HPV types 6 and 11 that are known to cause genital warts. Although the main protection for males is associated with genital warts, HPV-associated cancers in males include certain anal, penile, oropharyngeal, and oral cavity cancers primarily caused by the HPV-16. Therefore, there is an advantage for males as well in preventing as many types of HPV as possible.

It is recommended that children ages 11 and 12 be vaccinated before they become sexually active. The vaccines can be administered to children as young as 9 years of age. In addition, individuals between the ages of 13 and 26 should also be vaccinated as a sort of "catch-up" to try to cover as many people

(*continued*)

APPLICATION 16.1 *(continued)*

as possible against the virus (ACS, 2011). It is possible that the vaccines also could prevent some other HPV-related cancers such as those of the head and neck (ACS, 2011). Gardasil may be given to males aged 9 to 26 years to prevent genital warts. Both vaccines will prevent two types of HPV that cause most cervical cancers (HPV-16 and -18). They help prevent anal, vulvar, and vaginal cancers related to these two types of HPV as well. It is important to understand that once a person has become infected with the virus, the vaccine is no longer of any use: It can neither treat an established infection nor prevent cancer in someone who has the infection. The vaccine can only be used to prevent the initial infection. The vaccine is given in three doses as an IM injection over a 6-month period, with the second injection given 2 months after the first, and the third given at the 6-month date (CDC, 2012). The adverse effects that have been reported are injection-site reactions, headache, syncope, and fever that are common with other types of vaccine reactions.

Why is it important for the dental professional to be aware of this vaccine? Dental offices see many young children two or more times per year. Therefore, dental hygienists are in an excellent position to educate the parents of young girls/boys about this excellent opportunity to prevent a terrible disease. Many parents are not likely to think that they have to worry about their 11- or 12-year-old child being sexually active. However, this is not the point in question. The point is to vaccinate before there is any chance of exposure. Dental hygienists are also in a good position to talk to the 18- to 26-year-olds who may also want to take advantage of this vaccine and to discuss or answer questions that the parents of those under age 18 may have in the dental office. This topic may arise in the discussion regarding oral cancer and any HPV connection.

For more information on HPV vaccines, visit the following web sites:

Centers for Disease Control and Prevention: Human Papillomavirus (HPV) Infection
http://www.cdc.gov/std/treatment/2010/hpv.htm

Centers for Disease Control and Prevention: Cervical Cancer Statistics
http://www.cdc.gov/cancer/cervical/statistics/

American Cancer Society: Cervical Cancer Overview
http://www.cancer.org/Cancer/CervicalCancer/OverviewGuide/cervical-cancer-overview-key-statistics

American Cancer Society: Human Papilloma Virus (HPV), Cancer, HPV Testing, and HPV Vaccines — Frequently Asked Questions
http://www.cancer.org/acs/groups/cid/documents/webcontent/002780-pdf.pdf

Food and Drug Administration: Gardasil Prescribing Information
http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM111263.pdf

Additional information on the HPV vaccine may be obtained by calling 1-800-232-4636.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: Oral squamous papillomas manifest as painless, exophytic, well-circumscribed, pedunculated, or sessile masses. These masses may have a cauliflower-like surface texture or they may consist of many finger- or hair-like projections. They range in color from white to pink and can be found on the lips or any mucosal surface; however, they are seen more often on the soft palate, tongue, and lips (Fig. 16.1).

Distinguishing Characteristics: The cauliflower-like appearance of oral squamous papilloma suggests infection with HPV.

Significant Microscopic Features: The surface exhibits a proliferation of parakeratinized squamous epithelium with finger-like projections (Fig. 16.2).

Dental Implications: These lesions should be removed because of the association of some forms of HPV with oral malignancies and because the patient may be able to transmit the causal viral agent to others.

Differential Diagnosis: Any of the other forms of HPV infection need to be considered in a differential diagnosis, including the following:

1. Verruca vulgaris, Chapter 16
2. Condyloma acuminatum, Chapter 16
3. Verrucous carcinoma, Chapter 16
4. Focal epithelial hyperplasia, Chapter 16

Treatment and Prognosis: Conservative surgical excision usually suffices to treat this lesion. The risk of recurrence is low except in those individuals who are immunosuppressed and therefore have a considerably higher risk.

FIGURE 16.1. Oral squamous papilloma. The white finger-like projections covering the surface of this growth on the ventral surface of the tongue are characteristic of the squamous papilloma.

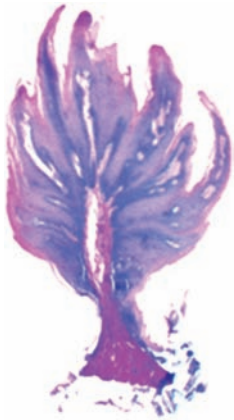

FIGURE 16.2. Oral squamous papilloma. Photomicrograph showing finger-like projections on a pedunculated lesion.

Verruca Vulgaris

The verruca vulgaris lesion is also known as the common wart. It can be caused by several of the HPVs, specifically 2, 4, 6, and 40 (all low-risk types). The virus enters through a break in the skin, and a wart forms. Oral lesions are usually caused by autoinoculation from the fingers to the mouth. Any time the clinician observes a verrucal–papillary lesion in the mouth, he or she should perform a quick examination of the patient's fingers for a similar lesion.

The virus enters the mucosa through a break in the surface epithelium usually caused by trauma. Figure 16.3 depicts multiple verrucae in a 9-year-old boy who had a habit of biting his cuticles and also had finger lesions. Surgical excision is the treatment of choice for these lesions. Approximately two-thirds of the lesions have been reported to disappear spontaneously, presumably because of the effectiveness of the patient's immune system in combating the virus.

NAME: Condyloma acuminatum (genital or venereal warts)

Etiology: Approximately 30 different types of HPV can infect the anogenital tract; however, HPV subtypes 6 and 11 (low-risk types) are the most common causes of this infection. HPV subtypes 16 and 18 (high-risk types) are less commonly associated with condyloma acuminatum (Higgins et al., 2006).

Method of Transmission: HPV is transmitted by direct (oral–oral or oral–genital) contact between the virus and compromised mucous membranes.

Pathogenesis: An estimated two-thirds of individuals who have sexual contact with an infected partner will develop genital warts, making this a highly infectious condition. The epithelial cells of the oral mucosal membranes or the mucosal membranes of the anogenital tract harbor the virus. Proliferation of the virus is related to the process of **keratinization** (production of keratin within the cells) (Regezi et al., 2008).

Extraoral Characteristics: These lesions can occur on any mucosal surface in the anogenital area. The clinical appearance is of multiple flat, pinkish, exophytic growths with sessile bases and rough cauliflower-like surfaces.

Perioral and Intraoral Characteristics: Intraoral lesions can be quite extensive and occur in those sites that are frequently traumatized during fellatio or cunnilingus, such as the labial and lingual frenula and the soft palate and oropharynx. However, almost any oral site can be affected. The lesions begin as papular growths that enlarge and coalesce, becoming nodular, pink, exophytic growths with a rough papillary surface (Fig. 16.4).

Distinguishing Characteristics: The cauliflower-like appearance of the lesion suggests an HPV infection.

Significant Microscopic Features: The surface of the lesion is covered by stratified squamous epithelium that is either **parakeratotic** (surface epithelial cells that have retained their nuclei) or nonkeratinized. There is marked thickening of the basal layer and the stratum spinosum of the epithelium (Fig. 16.5). A cervical smear exhibits koilocytes with a perinuclear halo and a wrinkled nucleus that contains viral particles. Koilocytes are epithelial cells that have a shrunken nucleus enveloped in large cytoplasmic vacuoles that contain HPV particles. The koilocyte occurs due to extensive

FIGURE 16.3. Verruca vulgaris. Multiple oral lesions in a 9-year-old who had similar lesions on his hands.

FIGURE 16.4. Condyloma acuminatum. Recurrent lesions exhibit the characteristic nodular growth with a rough papillary surface.

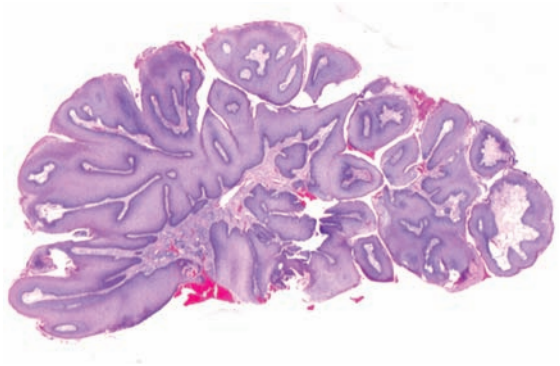

FIGURE 16.5. Condyloma acuminatum. Photomicrograph showing the histology of condyloma acuminatum. Note the more rounded projections of epithelium compared with the more pointed projections of the squamous papilloma.

replication of the virus, producing injury and resulting in the wrinkled appearance of the koilocyte (Rubin & Strayer, 2012).

Dental Implications: Diagnosis and treatment of this condition will help to prevent transmission of the virus. This infection is more common in immunosuppressed patients, and the clinician should carefully evaluate the patient's assessment data for other indications that would suggest the need for a medical referral.

Differential Diagnosis: Any of the verrucal–papillary lesions should be considered in a differential diagnosis. However, the flatter, less papillary appearance of this infection is more consistent with focal epithelial hyperplasia.

Treatment and Prognosis: Oral lesions are usually removed surgically using scalpel, laser, cryosurgery, or electrosurgery. Recurrences are common. Patients who are exposed to HPV-16 or -18 in the anogenital region have an increased risk of developing anogenital carcinomas. In addition, research has suggested a link between HPV-16 and oral and oropharyngeal carcinomas (Chung & Gillison, 2009; De Petrini et al., 2006; Ang et al., 2010, 2011; Gillison, 2007). Interestingly, these studies also suggest that the presence of HPV-16 in these cancers correlates with a better overall survival rate (Ritchie et al., 2003; De Petrini et al., 2006; Ang et al., 2011). The significance of this information is not clear, and more research is needed. Additionally, there is the question as to whether the HPV infection can be a sole etiologic factor in the development of SCC (Kumaraswamy & Vidhya, 2011).

NAME: Focal epithelial hyperplasia (Heck disease)

Etiology: HPV-13 and -32 (low-risk types) have been implicated in the development of this condition.

Method of Transmission: HPV-13 or -32 is transmitted in a manner similar to that of other HPVs, by surface contact with the virus through a break in the mucosal barrier. This is frequently due to localized trauma.

Epidemiology: Focal epithelial hyperplasia was first identified in 1965 in Native North Americans. It has since been identified in many population groups around the world. All ages can be affected, but the condition is somewhat more common in younger age groups. It affects both genders equally.

Pathogenesis: Introduction of the virus into the mucous membranes causes proliferation of the cells in the stratum spinosum.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: The lesions of focal epithelial hyperplasia display a pink-to-whitish, somewhat translucent, surface that is only slightly cauliflower-like. They are soft on palpation, as they generally have less keratin than the other HPV-related lesions. The lesions most commonly affect the lips, tongue, and buccal mucosa, where they appear as numerous discrete papular or nodular growths (Fig. 16.6).

Distinguishing Characteristics: These lesions may be more generalized within the oral cavity than the other forms of HPV.

Significant Microscopic Features: The hallmark of focal epithelial hyperplasia is the presence of **mitosoid figures** (cells in which the nuclear DNA has fragmented, resulting in a cell that appears as if it is undergoing mitosis) in the middle of the spinous layer of the epithelium (Fig. 16.7). These course, clumped chromatin bodies resemble a mitotic figure. These cells are referred to as mitosoid cells, mitosoid bodies, or mitosoid figures.

Dental Implications: None

Differential Diagnosis: All of the verrucal- or papillary-type lesions previously discussed would be considered in a differential diagnosis. In addition, the oral lesions associated with Cowden syndrome (see Chapter 17) and Crohn disease (see Chapter 10) may have a similar intraoral appearance, and they should also be considered.

Treatment and Prognosis: Treatment is not always necessary. Conservative excision may be preformed to establish a diagnosis. Often, these lesions will resolve spontaneously without any treatment. Malignant transformation is unlikely.

FIGURE 16.6. Focal epithelial hyperplasia. Lesions on the upper lip appear whitish, translucent, and much less papillary than other human papillomavirus (HPV)-related lesions.

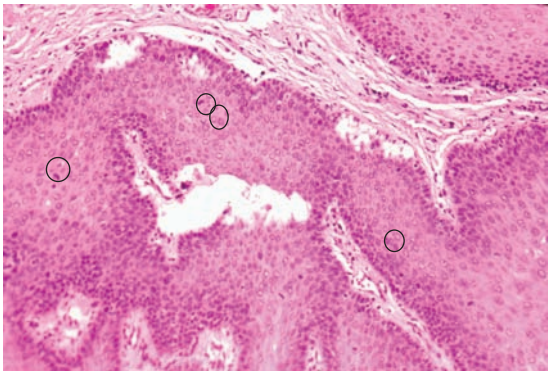

FIGURE 16.7. Focal epithelial hyperplasia. Photomicrograph showing mitosoid figures (*circled*) in the midspinous zone.

FIGURE 16.8. Papillary hyperplasia. This patient has been wearing a temporary partial to replace the maxillary incisors for several years. The poor fit associated with this type of prosthesis is often related to the development of papillary hyperplasia. Note the clusters of pink papules covering the surface of the hard palate.

Inflammatory or Reactive Lesions with a Papillary Configuration

Hyperplasia is a form of cellular adaptation to chronic injury. Often, this can produce a tissue mass that exhibits a rough or papillary surface. Most examples of reactive hyperplasias exhibit a smooth surface; however, it is not unusual to see some of these growths present with a somewhat rough or papillary surface. Most of these lesions are discussed under the clinical characteristics that they most often exhibit and are found within other chapters. One form of reactive hyperplasia, papillary hyperplasia, almost always exhibits a papillary surface and, therefore, is discussed in this section.

NAME: Papillary hyperplasia (inflammatory papillary hyperplasia)

Etiology: Papillary hyperplasia is a reactive tissue proliferation due to mild, persistent trauma caused almost exclusively by the rubbing of an ill-fitting denture on the mucosa during function.

Method of Transmission: Not applicable

Epidemiology: Papillary hyperplasia can occur in any age group but most often occurs in the elderly, because these patients are more likely to wear dentures, especially ill-fitting dentures. The longer a patient keeps a denture without having it evaluated for proper fit by a dentist, the more likely this lesion is to occur. The lesion occurs equally in both males and females.

Pathogenesis: Papillary hyperplasia develops over time, as a patient's denture becomes increasingly looser fitting as a result of the normal process of bone remodeling after loss of the teeth. As more and more bone is lost over time, the denture becomes increasingly likely to slip and rub during mastication. The chronic rubbing of the denture on the soft tissues of the mucosa overlying the bone results in a broad field of small papules in the areas directly beneath the denture. The condition is more common on the maxillary mucosa than on the mandibular mucosa, possibly because patients are more likely to keep their maxillary dentures in their mouths longer and because the maxillary denture covers a greater area of soft tissue.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: The lesion most commonly appears on the palatal mucosa as a field of pink-to-bright red, clustered papules that are firm to palpation (Fig. 16.8).

Distinguishing Characteristics: This condition is almost always related to the presence of dentures or oral appliances.

Significant Microscopic Features: A thickened or thinned epithelium covers cores of proliferative fibrovascular connective tissue. Numerous capillaries are present in the connective tissue. This, combined with thinned epithelium, results in a reddish appearance to the tissue (Fig. 16.9).

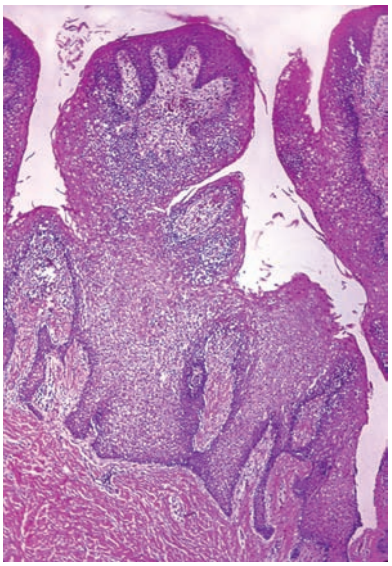

FIGURE 16.9. Papillary hyperplasia. Photomicrograph showing increased connective tissue rather than proliferating exophytic epithelium causing the papillary appearance. (Courtesy of Dr. Valerie A. Murrah.)

Dental Implications: Patients who exhibit this condition should be treated with a soft denture reline material prior to surgical removal of the lesion and fabrication of a new denture. They should also be educated on the proper use and care of their dentures, including the fact that dentures must be removed from the mouth for a period of time every day.

Differential Diagnosis: Although the clinical appearance of this lesion and its association with a denture or appliance strongly suggest papillary hyperplasia, other more serious conditions such as early verrucous carcinoma (see Chapter 16) must be considered and ruled out.

Treatment and Prognosis: The lesions should not be surgically excised without the fabrication of a new denture, since mechanical trauma related to functioning of an ill-fitting denture will simply result in recurrence. New dentures should never be fabricated over papillary hyperplasia, as the impressions for the new denture will incorporate the papillary configurations and will increase the likelihood that the new denture also will not fit well. Papillary hyperplasia is frequently associated with candidiasis, indicating that both the soft tissue and the denture surface need to be treated with an antifungal agent (refer to Clinical Protocol #5).

The prognosis is excellent, as long as new dentures are fabricated following removal of the lesion and the patient is educated about the necessity of periodic evaluations to check the fit of the denture and the health of the underlying mucosa.

Premalignant/Malignant Lesions Associated with a Rough or Papillary Surface

The genetic material of the high-risk HPV types 16 and 18 is typically added or combined with the host's DNA in malignant lesions. Integration of the viral DNA into the host cell's DNA is considered a hallmark of malignant transformation (Gearhart et al., 2006). Proteins made by the viral DNA of high-risk types have been shown to inactivate the host's tumor suppressor proteins, resulting in unregulated host cell proliferation and malignant transformation. Two conditions are discussed in this section. Keratoacanthoma is considered a benign or premalignant lesion even though it exhibits some characteristics associated with a malignant lesion. Verrucous carcinoma is a low-grade epithelial malignancy.

NAME: Keratoacanthoma

Etiology: The exact cause of keratoacanthoma is not clear. Keratoacanthomas are somewhat controversial lesions in that some experts regard them as benign and others regard them as a low-grade variant of invasive SCC (Chuang & Brashear, 2006; Ko, 2010). Further investigation is needed.

Exposure of the affected area to sunlight is strongly associated with the development of this lesion. Other possible factors include the presence of chromosomal abnormalities in the skin, occupational exposure to tar and/or pitch, a compromised immune status, and exposure to several forms of HPV, including types 9, 11, 13, 16, 18, 24, 25, 33, 37, and 57.

Epidemiology: The peak incidence of this lesion occurs in those over the age of 60 years. It is rarely found in anyone under the age of 20. It is uncommon in darker skinned individuals and is seen more often in males than in females (Chuang & Brashear, 2006).

Pathogenesis: These lesions originate from the pilosebaceous glands (sebaceous glands associated with hair follicles). The lesions are usually solitary and begin as firm, skin-colored, or reddish papules that rapidly progress to dome-shaped nodules, about 1 to 2 cm in size, over a period of several weeks. This tumor frequently undergoes spontaneous regression (Ramos et al., 2009).

Extraoral Characteristics: Most keratoacanthomas arise on the sun-exposed skin of the face, neck, and upper extremities. The dome-shaped nodules display a smooth shiny surface with a central crater containing a core or plug of keratin.

Perioral and Intraoral Characteristics: Keratoacanthomas are most frequently detected by the dental team on the edge of the vermilion border of the lower lip (Fig. 16.10). These lesions are not found on mucous membranes within the oral cavity.

Distinguishing Characteristics: The clinical appearance and location of the keratoacanthoma may help to differentiate it from other lesions. However, the uncertain relationship between this and SCC indicates the need for prompt identification and treatment.

Significant Microscopic Features: The keratoacanthoma is a symmetrical lesion of well-differentiated squamous epithelium. There is cupping of the edges of the normal epidermis

FIGURE 16.10. Keratoacanthoma. Note the keratin within the central area of the lesion. (Courtesy of Dr. Amy Brooks.)

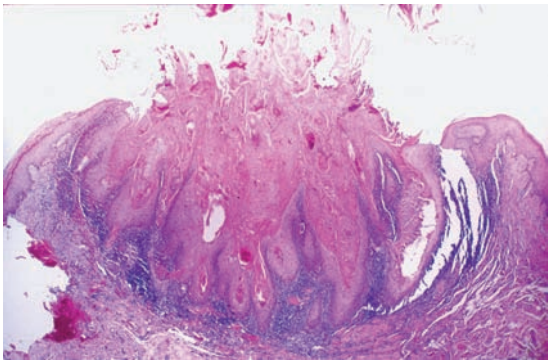

FIGURE 16.11. Keratoacanthoma. Note the cup-shaped appearance, central keratin, and the extensive infiltrate of inflammatory cells below the epithelium. (Courtesy of Dr. Valerie A. Murrah.)

that extends over a central crater filled with keratin. A prominent inflammatory cell infiltrate is present in the dermis, adjacent to the invading epithelium of the lesion (Fig. 16.11). Of utmost importance is the histologic similarity between the keratoacanthoma and well-differentiated, low-grade SCC, which makes distinguishing between the two difficult at the very least (Ko, 2010).

Dental Implications: Observation of a lesion with this general appearance during an extraoral examination should prompt a medical referral by the dental health care provider. In addition, patients who develop keratoacanthomas are at higher risk for developing subsequent nonmelanoma skin cancer; therefore, patients should be educated about prevention and self-examination. Refer to Clinical Protocol #10 for information related to preventing skin cancer.

Differential Diagnosis: The differential diagnoses of keratoacanthoma in its typical location on the lower lip include the following:

1. Recurrent herpes labialis, Chapter 11
2. Syphilitic chancre, Chapter 12
3. Squamous cell carcinoma, Chapters 5 and 12
4. Actinic cheilitis, Chapter 14

Treatment and Prognosis: Surgical excision is the treatment of choice. Since the biologic behavior of an individual keratoacanthoma cannot be predicted, many dermatologists advocate that treatment of keratoacanthoma be equivalent to treatment for SCC (Chuang & Brashear, 2006). The prognosis is excellent with complete surgical removal. Untreated lesions may regress spontaneously, leaving a scar.

NAME: Verrucous carcinoma

Etiology: Most verrucous carcinomas appear to be related to the use of spit tobacco, either snuff or chewing tobacco. Spit tobacco contains various carcinogens including polonium-210, tobacco-specific *N*-nitrosamines, volatile aldehydes, and polycyclic aromatic hydrocarbons. Smokeless tobacco products are a major source of cancer-causing nitrosamines and a known cause of human cancer. They increase the risk of developing oral cancer, esophageal cancer, and cancer of the pancreas (Cancer Prevention & Early Detection Facts and Figures, 2010). Mucous membrane exposure to alcohol also appears to be a factor in the etiology of verrucous carcinoma. In addition, several forms of HPV have been found within lesions of verrucous carcinoma (see Clinical Protocol #24).

Method of Transmission: Verrucous carcinomas are not thought to be contagious, although a variety of HPV types have been localized within them.

Epidemiology: Verrucous carcinoma occurs primarily in males over the age of 55. Between 1985 and 1996, The National Cancer database showed only 0.6% of the 411,534 cases of head and neck carcinoma to be designated as verrucous carcinoma (Koch et al., 2001). However, it is estimated that 7 to 13 million people use spit tobacco in the United States every year, making the potential for the development of this lesion significant (Dolev & Kimball, 2006).

Pathogenesis: Verrucous carcinoma most often develops at the site of placement of the tobacco quid. This association is so strong that this type of carcinoma has often been termed "snuff dippers' cancer" when it appears in the oral cavity. Verrucous carcinomas are slow-growing lesions. Although they invade adjacent structures, they do not tend to metastasize.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: Early lesions appear as white patches, whereas more fully developed lesions display a cauliflower-like papillary appearance that spreads over a large area of the mucosa. There may be fissuring and ulceration of the lesions. In addition, SCCs have been reported to develop within verrucous carcinoma lesions. Verrucous carcinoma is usually found on the vestibular mucosa, alveolar ridge, and gingiva, as well as the buccal mucosa (Fig. 16.12).

FIGURE 16.12. Verrucous carcinoma. Verrucous carcinoma of the left buccal mucosa in a male patient who was a longtime tobacco chewer and smoker. Note the areas of leukoplakia surrounding the lesion.

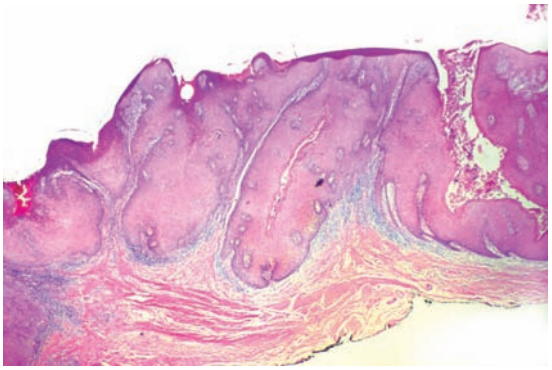

FIGURE 16.13. Verrucous carcinoma. Photomicrograph showing the invagination of epithelium, the invasive downgrowth of the epithelium, and the chronic inflammatory cells just below the invading epithelium.

Distinguishing Characteristics: The general appearance of verrucous carcinoma coupled with a history of spit tobacco use suggests this lesion; however, a biopsy must be performed for a definitive diagnosis.

Significant Microscopic Features: The lesion displays a highly keratinized surface that is undulating and markedly papillary, with deep invaginations of the mucosa (Fig. 16.13). In most cases, one observes a chronic inflammatory cell infiltrate immediately adjacent to the margins of the invading neoplasm.

Dental Implications: Verrucous carcinoma often forms within long-standing leukoplakia associated with spit tobacco. The dental hygienist is in an excellent position to educate patients about the effects of spit tobacco use and counsel them about tobacco cessation.

Differential Diagnosis: Any of the papillary lesions are included in a differential diagnosis of verrucous carcinoma, including the following:

1. Condyloma acuminatum, Chapter 16
2. Oral squamous papilloma, Chapter 16
3. Verruca vulgaris, Chapter 16
4. Leukoplakia, Chapter 14

Treatment and Prognosis: Surgical removal is the treatment of choice. Cryotherapy (freezing) also has a high cure rate for well-circumscribed lesions. Most patients have a good prognosis, as metastasis is rare. However, if SCC is identified within the verrucous carcinoma, the prognosis becomes much less favorable.

SUMMARY

- HPV is the primary etiologic agent associated with verrucous or papillary lesions. There are well over 140 different types of HPV infectious agents.
- Low-risk HPV types are associated with benign epithelial lesions, while high-risk types are associated with malignant lesions, such as verrucous carcinoma and SCC.
- Oral squamous papillomas are associated with low-risk HPV types and can be spread by autoinoculation. They appear as exophytic, pedunculated, or sessile masses covered with finger-like projections.
- Verruca vulgaris (common wart) can present in the oral cavity and is usually associated with autoinoculation from a lesion on the hands.
- Condyloma acuminatum is an STD that is caused by 30 or more types of HPV. The lesions can affect the genitals and/or the mouth, depending on where the virus contacts the skin. Infection with high-risk types of HPV and retention of the virus within the cells increase the individual's risk of developing SCC in the future.
- Over 90% of cases of cervical cancer are caused by high-risk HPV. A vaccine to prevent infection with specific HPV types (6, 11, 16, and 18) is available. The vaccine can prevent 100% of infections with HPV-16 and -18 and 99% of infections with HPV-6 and -11.
- Focal epithelial hyperplasia presents in the oral cavity as numerous discrete papular or nodular growths that are much less papillary than other lesions caused by HPV. Numerous mitosoid figures in the stratum spinosum of the epithelium are characteristic microscopic features of this disorder.
- Papillary hyperplasia is an inflammatory lesion caused by wearing an ill-fitting denture. It may be accompanied by an infection with *Candida albicans*. The lesion must be removed before a new denture can be made.
- The keratoacanthoma is a lesion that originates in a pilosebaceous gland. Its development is associated with exposure to sunlight and some forms of HPV, among other factors. This lesion is histologically very similar to SCC, and experts are undecided as to whether this is actually a low-grade form of SCC or a benign lesion. The lesion appears as a papule that rapidly grows to form a dome-shaped nodule with a central plug of keratin. The lesion usually regresses without treatment; however, patients who have had keratoacanthoma have a higher risk of developing skin cancer in the same area.
- Verrucous carcinoma is a slow-growing epithelial malignancy cancer that invades local structures but does not tend to metastasize. These cancers often develop in a preexisting leukoplakia that is associated with spit tobacco use. In addition, HPV has been found within the lesions, possibly linking this form of cancer to an infection with HPV. SCC development also has been observed within these lesions.

CHAPTER REVIEW

Case Study 16.1

A 45-year-old male, Mr. G, arrives at your office for a routine checkup and prophylaxis. He complains of a white bump that has never been there before. He admits to picking off portions of the bump, but it always comes back to its previous size; in fact, it seems to the patient that the lesion has recently been increasing in size. The patient is not quite sure how long the lesion has been present but says that he thinks it is approximately 6 months, because he was sure it was not present at the last dental appointment. You confirm this by reviewing the chart notes of the previous appointment, as your office prides itself on meticulous notes regarding maintenance examinations. The patient indicates that the lesion is nonpainful but is bothersome to him, and he feels it may "show" when he speaks. You listen intently and tell Mr. G that his complaint will be addressed as soon as you have completed your assessment. The extraoral examination is unremarkable except for the lesions pictured in Figure 16.14. During the intraoral examination, you note a white papillary lesion on the mucosal portion of the right lower lip (Fig. 16.15).

1. What are the critical parts of the health history that you would want to review at this point?
2. Develop a differential diagnosis for this lesion.
3. What part do your extraoral findings play in determining a differential diagnosis?
4. What do you think the most likely diagnosis for the oral lesion will be when it is biopsied?

FIGURE 16.14. Extraoral findings.

FIGURE 16.15. Intraoral findings.

For answers and additional review activities, log in to **thePoint.lww.com**

CASE STUDY 16.2

The patients in Figure 16.16 have well-circumscribed raised lesions located on the midline, at the tip of the tongue. Assessing these lesions, answer the following questions.

1. Write a description of the growths depicted in Figure 16.16.
2. Which category would you consider in your assessment of these lesions?
   - a. Inflammatory
   - b. Immune system related
   - c. Neoplastic
   - d. Genetic
   - e. Infectious
   - f. Traumatic
3. What do you think may cause such a growth? List your differential diagnosis.
4. Do you think that this growth will resolve without any treatment?
5. Do you think that this growth could be a malignancy?
6. Do you think that this could be caused by a habit resulting in trauma to the area?
7. What features make you believe that this could be benign or malignant?

FIGURE 16.16. Firm, circumscribed, sessile-based tissue growth at the midline of the tongue, approximately 4 × 3 mm with smooth surface and uniform in color. (Courtesy of Sherri M Lukes, RDH, MS.)

For answers and additional review activities, log in to **thePoint.lww.com**

Critical Thinking Activity

A 70-year-old male and 50-year spit tobacco user displays a rough white verrucous lesion of the mandibular vestibule measuring 2.0 × 2.5 cm. The lesion is very firm to palpation. The patient doesn't want to quit his habit.

1. Should the practitioner ask the patient to move his quid of spit tobacco around to different places in the vestibule and then have the patient return in 2 weeks to look for regression?
2. In what situation, if any, would this type of recommendation be appropriate?
3. Could some method other than a biopsy be recommended to determine the identity of a thick verrucous white lesion found on the oral mucosa?

Portfolio Activities

- Construct separate patient education sheets for patients with verruca vulgaris, condyloma acuminatum, and inflammatory papillary hyperplasia. Describe the causes of these conditions in terms that are easily understandable. Delineate the reason(s) that surgical treatment(s) is(are) required. Finally, discuss appropriate lifestyle changes that will prevent the patient from acquiring recurrences of the lesions. These may include smoking cessation, alcohol cessation, nutrition, stress reduction, and exercise to maintain a healthy lifestyle.
- Construct a pamphlet for education of high school students concerning oral lesions caused by HPV. Include information about HPV transmissibility and the use of smokeless tobacco in the etiology of verrucous carcinoma.
- Write a patient information pamphlet on appropriate denture care. In it, discuss the interrelationship between loose dentures and papillary hyperplasia, the ill effects of leaving one's dentures in at night, and the sequelae of failing to get periodic oral examinations by a dentist despite the fact that the patient no longer has teeth.

Media Menu

Web Sites

American Cancer Society
www.cancer.org

American Social Health Association
www.ashastd.org

Cancer*Care*
www.cancercare.org

Centers for Disease Control and Prevention: National Breast and Cervical Cancer Early Detection Program (NBCCEDP)
www.cdc.gov/cancer/nbccedp/index.htm

Study Tools

Take advantage of additional online resources to help you study and ace your exams!

- Answers to case studies in the book
- Additional case studies and answers
- Interactive quiz bank with answer feedback
- Fully searchable e-book for quick lookup and studying on-the-go
- Expanded Media Menu with direct links to related Web sites and multimedia resources
- Supplemental References

thePoint Online resources and links are available at http://thepoint.lww.com/DeLong2e.

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NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Oral Squamous Papilloma	Human papillomavirus (HPV) 2, 6, 11, and 57	Arise from the proliferation of infected basal keratinocytes	Painless, exophytic well-circumscribed, pedunculated or sessile masses. Cauliflower-like surface. White or pink color on any mucosal surface.	Microscopically exhibit parakeratinized squamous epithelium with finger-like projections	Surgical excision	Recurrence may be more likely in immunocompromised patients.
Verruca Vulgaris	Caused by HPV-2, -4, -6, -40 (all low-risk types)	Virus enters the mucosa through a break in the surface epithelium. Can occur through autoinoculation.	Typical wart-like appearance with rough papillary appearance	Microscopically exhibit squamous epithelium with finger-like projections	Excision may be needed but 2/3 disappear spontaneously.	Patients should be told how to avoid selfinoculation such as transferring virus from hands to mouth.
Condyloma Acuminatum (Genital or Venereal Warts)	HPV type 6 and type 11. Less common is HPV-16 or -18.	Two-thirds of individuals who have sexual contact with an infected partner will contract the virus.	Multiple flat, pinkish, exophytic growths with sessile base and rough cauliflower-like surfaces	Surface covered by stratified squamous epithelium. Marked thickening of the basal layer and epithelium. Koilocytes are noted. These occur due to extensive replication of the virus.	Removal with scalpel, laser, cryosurgery, or electrosurgery	Diagnosis and treatment will help prevent transmission. Carefully evaluating the etiology of the lesions is needed since medical referral may be needed. If HPV-16 is detected, there is a higher risk of anogenital carcinoma and oropharyngeal carcinoma.
Focal Epithelial Hyperplasia (Heck Disease)	HPV-13 and/or -32 (low-risk types)	Introduction of the virus into the mucous membranes causing proliferation of the keratinized cells in the stratum spinosum	Display a pink to whitish somewhat translucent surface with slight cauliflower-like appearance. Nodular or papular growths. Soft on palpation. Most commonly affect lips, tongue, and buccal mucosa.	Mitosoid figures—cells appear to have DNA fragmentation and appear to be undergoing mitosis.	May require conservative excision or may require no treatment depending upon the individual case	None
Papillary Hyperplasia (Inflammatory Papillary Hyperplasia)	Reactive tissue proliferation to mild, persistent trauma	Usually caused by chronic friction from an ill-fitting denture	Usually occurs on the palate as a field of pink-to-bright red, clustered papules that are firm to palpation	Thickened or thinned epithelium covers cores of proliferative fibrovascular connective tissue. Numerous capillaries are present in the connective tissue. The epithelium is thinned with a reddish appearance.	Other more serious disease states such as verrucous carcinoma must be considered and ruled out.	The patient should be treated with a soft denture reline material prior to any surgical removal of the lesion and a new denture. Dentures should never be remade until the existing hyperplasia is corrected. Prognosis is excellent.
Keratoacanthoma	Etiology is unknown. Some associate these with squamous cell carcinoma.	Sunlight is strongly associated with these as are chromosomal abnormalities in the skin, exposure to tar or pitch, lowered immune system, and HPV infection. The lesions originate from sebaceous glands in hair follicles.	Usually solitary, and begin as firm, skin-colored or reddish papules progressing to domed nodules about 1–2 cm. Most occur in males and arise in sun-exposed skin of the face, neck, and upper extremities. High area of occurrence is the lower lip.	Squamous epithelium that is cupped on the edges of the normal epidermis. A prominent inflammatory exudate is present in the dermis. There is a strong appearance to squamous cell carcinoma. A central core of keratin is noted.	The appearance of low-grade well-differentiated squamous cell carcinoma and the keratoacanthoma is very difficult in most cases to discern. Careful examination by a pathologist is needed. Surgical excision is needed and most pathologists treat lesions as if they are squamous cell carcinoma.	The patient should be educated about prevention and self-examination. These patients are at a high risk for development of melanoma.
Verrucous Carcinoma	Usually related to spit tobacco, snuff, or chewing tobacco	Content of specific carcinogens related to products in tobacco. Alcohol and HPV are associated as well.	White patches with more fully developed lesions appearing more cauliflower-like.	Highly keratinized surface with markedly papillary surfaces including deep invaginations. A chronic inflammatory infiltrate is evident at the margins of the invading neoplasm.	Long-standing leukoplakia is usually evident and the hygienist is in a prime position to provide tobacco cessation instructions to the patient or to make a referral to a smoking cessation facility.	Any leukoplakia should receive a diagnosis, and surgical excision is needed to remove the verrucous carcinoma. Cryotherapy has a high cure rate for well-circumscribed lesions.

CHAPTER 17

Soft Tissue Enlargements

KEY TERMS

Acinic cell carcinoma	Mycobacteria
Adenoid cystic carcinoma	Myoepithelial
Adjuvant therapy	Neurilemoma
Bacterial sialadenitis	Neurofibroma
Café au lait macule	Oophoritis
Cervical lymphoepithelial cyst (branchial cyst)	Orchitis
Choristoma	Parotitis
Cowden syndrome	Perineural invasion
Crepitus	Peripheral fibroma
Cyst	Photophobia
Cystic hygroma	Pleomorphic adenoma
Dysphonia	Polymorphous low-grade adenocarcinoma
Fibroma	Proliferation
Fibromatosis	Ranula
Fibrosarcoma	Rhabdomyosarcoma
Fluctuant	Sarcoidosis
Foliate papilla	Sjögren syndrome
Frey syndrome	Syndrome
Gingivectomy	Teratoid cyst
Glands of Blandin-Nuhn	Thyroglossal tract cyst
Hamartoma	Traumatic neuroma
Keratoconjunctivitis sicca	Trismus
Leiomyoma	Warthin tumor
Lymphangiomas	Xerophthalmia
Lymphoid hyperplasia	Xylitol
Mucoepidermoid carcinoma	

LEARNING OUTCOMES

1. Define and use the key terms listed in this chapter.
2. Identify the different types of processes associated with the development of soft tissue enlargements.
3. Identify the extraoral manifestations associated with Cowden syndrome, sarcoidosis, Sjögren syndrome, neurofibromatosis, MEN type IIIB, and lymphangiomas.
4. Identify distinguishing characteristics for traumatic neuroma, denture-induced fibrous hyperplasia, peripheral ossifying fibroma, generalized gingival hyperplasia, bacterial sialadenitis, Sjögren syndrome, minor salivary gland tumors, neurofibromatosis, and lymphangioma.
5. Name three medications that are associated with the development of gingival hyperplasia.
6. Identify the circumstances under which traumatic or inflammatory lesions have the highest potential for recurrence after surgical removal.
7. Describe the role of dental biofilm in exacerbating the hyperplastic process that takes place in generalized gingival hyperplasia.
8. List the structures in the oral cavity that are most likely to contain hyperplastic lymphoid tissues.
9. Identify the complications associated with mumps.
10. Discuss treatment options for Sjögren syndrome and other forms of xerostomia.
11. List the soft tissue tumors that occur most frequently on the tongue.
12. Identify the most common soft tissue sarcoma found in children.
13. Discuss complications of parotid gland surgery or removal, including Frey syndrome.
14. Differentiate salivary gland tumors according to whether they arise more frequently in the major or minor salivary glands.
15. State the diagnostic criteria for neurofibromatosis.
16. Describe the malignant conditions associated with neurofibromatosis, MEN III syndrome, and Cowden syndrome.
17. Identify the soft tissue neoplasms for which adjuvant radiation or chemotherapy is often recommended.

CHAPTER OUTLINE

Traumatic or Inflammatory Lesions
- Traumatic neuroma
- Fibroma
- Cowden syndrome
- Peripheral ossifying fibroma
- Generalized gingival hyperplasia
- Lymphoid hyperplasia
- Sarcoidosis
- Ranula

Infections
- Mumps
- Bacterial sialadenitis

Immune System Disorders
- Sjögren syndrome

Soft Tissue Neoplasms
- Fibromatosis
- Fibrosarcoma
- Neurilemoma
- Neurofibroma

Neoplasms of Smooth Muscle
Neoplasms of Striated Muscle Cells
- Rhabdomyosarcoma

Neoplasms of Fat Tissue
Salivary Gland Neoplasms
- Pleomorphic adenoma
- Carcinoma ex-mixed tumor
- Frey syndrome
- Papillary cystadenoma lymphomatosum
- Mucoepidermoid carcinoma
- Acinic cell carcinoma

Minor Salivary Gland Malignancies
- Polymorphous low-grade adenocarcinoma
- Adenoid cystic carcinoma

Genetic and Congenital Disorders
- Neurofibromatosis
- Multiple endocrine neoplasia syndrome
- Lymphangioma

Soft Tissue Developmental Cysts
- Cervical lymphoepithelial cyst
- Thyroglossal tract cyst
- Dermoid cyst

RELATED CLINICAL PROTOCOLS

#1 Performing a Cytology Smear
#2 Applying Topical Corticosteroids in the Mouth
#3 Maintenance Appointment Guidelines for the Patient with a Mucosal Disorder
#4 Treating Patients with Xerostomia
#11 Patient Education: Oral Cancer Self-Examination
#12 Adjunctive Oral Premalignant Screening Devices
#14 Postoperative Instructions for Oral Surgery Patients
#17 Oral Health Care Management for the Patient with Heart Disease
#19 Oral Health Care Management for the Patient with Cancer
#21 Oral Health Care Management for the Patient Taking Anticoagulant Medications
#24 Tobacco Cessation
#25 How to Utilize Nutrition Counseling in Practice
#28 Saliva Testing

This chapter introduces the clinical, microscopic, and diagnostic aspects of both benign and malignant soft tissue enlargements. Soft tissue enlargements originate from several sources, some of which include epithelial tissue, connective tissue, and neural tissue. Some of the lesions are traumatic or reactive, which means they are associated with an inflammatory process. Others are associated with a neoplastic process, which can be caused by inherited mutations. They may also be associated with genetic damage from an environmental source or from a change in the individual's ability to repair damaged DNA or suppress tumor formation. Still others are developmental, or caused by an error in morphogenesis, the abnormal development of a tissue or organ. Often, these mimic a neoplastic process, but they are not true neoplasms because they do not exhibit uncontrolled growth. Instead, they grow as the individual grows, in a pattern that is consistent with the specific tissue. The descriptive name, **hamartoma,** is given to a lesion comprising an excessive abnormally arranged mass of normal tissue at any given site. For example, vascular tissues are normally found all over the body, but a vascular malformation (see Chapter 13) is a disarrayed mass of vascular tissues and is therefore a hamartoma. The term **choristoma** is given to this type of lesion when it occurs as a well-formed entity in an area where it would *not* be expected to be found. For example, Fordyce granules are well-formed sebaceous glands that develop within the buccal mucosa, which is not where they are customarily found. Developmental anomalies are often present at birth (congenital) or they may develop as the individual ages.

Soft tissue enlargements exhibit a wide variety of clinical manifestations. Large lesions may be clinically visible, while smaller lesions may only be detectable when palpated. The art of palpation must be developed over time so the clinician is able to reliably distinguish normal from abnormal (See Application 17.1). Occasionally, specific lesions are associated with very distinct characteristics that help to differentiate them from other lesions. More often, soft tissue enlargements exhibit a generic clinical appearance that offers little direction toward discovering a diagnosis. Because of this, most soft tissue enlargements require a biopsy to determine a definitive diagnosis.

Traumatic or Inflammatory Lesions

Hyperplastic traumatic or inflammatory lesions are usually associated with a specific cause or event that initiates an adaptive response in the tissues that initiates enlargement (see Chapter 2). The cause can be as simple as a cheek bite or an ill-fitting denture that causes chronic irritation, or it can be complex, such as extensive facial trauma related to a motor vehicle accident. In any case, hyperplastic tissue forms as an overexuberant response to the injury. The disorders in this section are all associated with acute or chronic trauma or inflammation.

APPLICATION 17.1

Palpation is defined as using the sense of touch to examine anatomic structures or areas for size, shape, consistency, texture, and other characteristics. This is a learned skill that must be practiced many times before a clinician can feel somewhat confident about his or her findings. It is important to develop a systematic method for palpating the structures of the head, neck, and oral cavity. Some suggestions for this are outlined in Chapter 1. Clinicians should be looking for the following while performing palpations:

- Differences (size, shape, consistency, and texture, among others) between structures that occur on opposite sides. For example: Submandibular lymph nodes on the right side may be enlarged, while those on the left are nonpalpable, or the left parotid gland may be hard or doughy to palpation, while the right gland is not. These differences could be significant and should be noted.
- Tenderness. Before beginning palpation, the clinician should ask the patient to report any feelings of tenderness or pain. In addition, it may be helpful for the patient to report any sort of difference between sensations felt in one area and those felt in other areas. Problems associated with nerve damage, such as paresthesia, may be discovered in this fashion.
- Variations in temperature. Be aware of the temperature of structures as they are palpated. A rise in the temperature can indicate increased blood supply to the area and may be associated with abnormalities, such as vascular malformations or infections.
- Alterations in color. Color changes during palpation of an area should also be noted. Color changes can indicate a vascular lesion or perhaps an inflammatory reaction if the tissue blanches upon palpation.
- Sounds. The clinician should be aware of any sounds that are produced when tissues are palpated. Fluid movement from one part of a lesion to another may cause a crackling sound, or crepitus.

Identification of abnormalities during palpation is just the first step. Formulating a differential diagnosis is the next step. The process then of determining a definitive diagnosis from a differential diagnosis is discussed in Chapter 1.

NAME: Traumatic neuroma

Etiology: **Traumatic neuromas** result from chronic or acute trauma that severs nerve tissue. One of the most common causes of traumatic neuroma in the oral cavity is the injection of local anesthetics prior to dental procedures. Surgical procedures such as tooth extraction may also be associated with development of a traumatic neuroma.

Method of Transmission: Not applicable

Epidemiology: Neuromas can occur in any age group, but most often occur in adults.

Pathogenesis: Trauma to the nerve is followed by ineffective unregulated nerve regeneration, which results in enlargement.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: Traumatic neuromas appear as small firm nodules covered by normal mucosa. The nodules are usually painful when palpated but otherwise may produce no symptoms. These lesions are found most often on surfaces that are traumatized frequently, such as the tongue, lower lip, and alveolar ridge or in the area of the mental foramen (Fig. 17.1).

Distinguishing Characteristics: Although not always present, pain on palpation is characteristic of this lesion and may help to differentiate it from similar lesions.

Significant Microscopic Features: Irregular nerve bundles can be seen within dense fibrous connective tissue. Inflammatory cells are rarely seen within the lesion.

Dental Implications: Careful avoidance of the area during dental or dental hygiene therapy is indicated to reduce the chance of eliciting or exacerbating pain.

Differential Diagnosis: The appearance of this lesion is similar to that of many of the other soft tissue enlargements; thus, biopsy is necessary for a definitive diagnosis. The presence of pain on palpation should make the clinician suspect a traumatic neuroma, especially if there is a history of trauma. The following lesions should be considered in a differential diagnosis:

1. Neurofibroma, Chapter 17
2. Neurilemoma, Chapter 17
3. Fibroma, Chapter 17

Treatment and Prognosis: Surgical removal of the neuroma is the usual treatment. There is a low rate of recurrence;

FIGURE 17.1. Traumatic neuroma. Careful examination of the lower vestibule detected the small nodular growth depicted in this photograph. Microscopic examination determined this to be a neuroma. (Courtesy of Dr. James Sciubba.)

therefore, the prognosis is excellent. In some cases, pain persists even after surgical removal of the neuroma.

NAME: Fibroma (focal fibrous hyperplasia, irritation fibroma, traumatic fibroma)

Etiology: **Fibromas** are not considered true neoplasms, but rather reactive responses to chronic trauma or irritation. One specific form of this condition is called "denture-induced fibrous hyperplasia" (sometimes called epulis fissuratum) and results from wearing an ill-fitting denture.

Method of Transmission: Not applicable

Epidemiology: Fibromas are the most common tumors found in the oral cavity. The peak incidence of this lesion occurs in the fourth to sixth decades, and it is seen more frequently in females than in males. Denture-induced fibrous hyperplasia is seen more often in the older population, since this condition only occurs in patients who wear dentures. Older patients in nursing homes are particularly vulnerable, since dental care is not always provided in these facilities.

Pathogenesis: Chronic or recurrent trauma causes a reactive hyperplasia, resulting in a fibrous connective tissue enlargement that appears similar to the surrounding tissues. The affected areas are frequently retraumatized, adding to the **proliferation** (growth) of the tissues.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: The growths are usually nodular and exophytic. They may be pedunculated. They have a smooth surface texture and firm consistency, and are about the same color or slightly lighter in color than the surrounding tissues. The surface of the lesion may be ulcerated if it is continually traumatized. Although the lesions can be found on any mucosal surface, they are usually found in areas of the oral cavity that are frequently traumatized, such as the tongue, buccal mucosa, and lips (Fig. 17.2). Figure 17.3 shows a fibroma in the palatal region. Denture-induced fibrous hyperplasia is characterized by exuberant growth of tissue under and around a denture, often involving the tissues in the vestibule. The tissue normally takes on a folded appearance, with the flange of the denture fitting between the folds (Fig. 17.4).

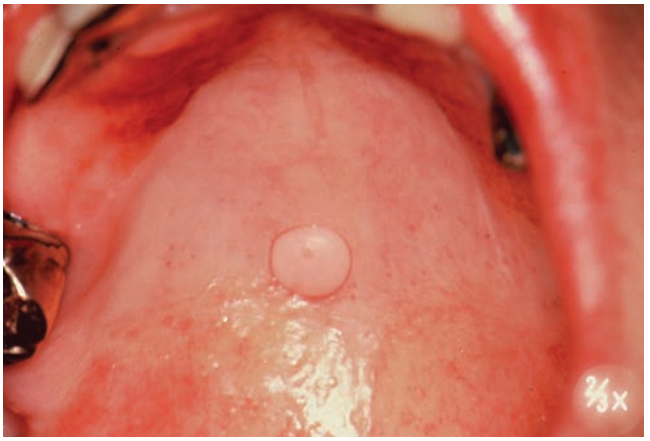

FIGURE 17.3. This fibroma has developed on the hard palate.

Distinguishing Characteristics: Fibromas can look like any other soft tissue tumor. However, denture-induced fibrous hyperplasia is always associated with a denture, which can help in developing a differential diagnosis.

Significant Microscopic Features: The histologic appearance is that of a nodular excess of collagen fibers with sparse amounts of inflammatory cells.

Dental Implications: The most important dental implication is determining the cause of the irritation or trauma and removing it. Removing the source will not result in complete resolution of the lesion but may result in reduction in size because of a reduction in the amount of inflammation present in the tissue.

Patients who have dentures should be advised to seek routine dental care in the form of soft tissue examinations and oral cancer screenings. In addition; dentures do not "fit" an individual for the rest of his or her life; the alveolar

FIGURE 17.2. Fibromas are found in areas that are frequently traumatized, such as the lip in this picture. (Courtesy of Dr. Michael Brennan.)

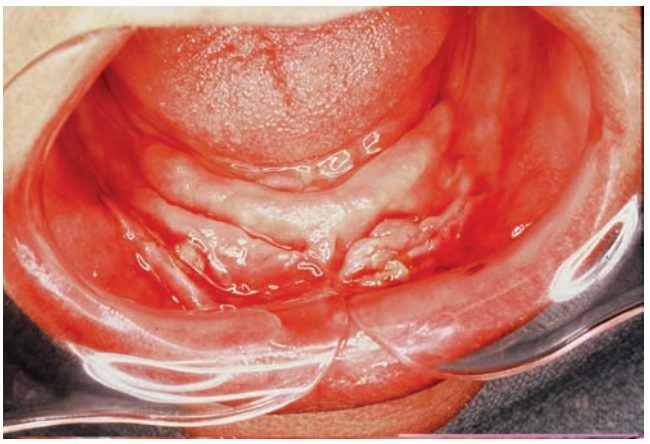

FIGURE 17.4. Denture-induced fibrous hyperplasia. Note the folds of fibrous tissue within which the flange of the mandibular denture rests.

bone remodels over time, and the denture teeth wear down from use, so they need to be evaluated routinely for fit and function. Eventually, all dentures must be relined or replaced. Wearing the denture too often also plays a part in the development of denture-induced fibrous hyperplasia. Dentures should always be left out of the mouth for a period of time every day. One of the problems associated with denture-induced fibrous hyperplasia is the tendency for these areas to develop fungal infections (candidiasis) that require treating the denture along with the soft tissue. Patients should be shown how to care for their dentures and for the soft tissues that support them. Refer to Clinical Protocol #11 for information about how to care for a denture.

Differential Diagnosis: The traumatic fibroma is clinically similar to many of the other soft tissue enlargements. A definitive diagnosis depends on histologic findings after a biopsy. Some of the most likely lesions in the differential diagnosis include the following:

1. Neurofibroma, Chapter 17
2. Neurilemoma, Chapter 17
3. Lipoma, Chapter 17
4. Peripheral ossifying fibroma, Chapter 17

The surface of denture-induced fibrous hyperplasia may be rough or papillary, in which case it can resemble verrucous carcinoma (see Chapter 16) or verruca vulgaris (see Chapter 16).

Treatment and Prognosis: Surgical removal of the fibroma is the treatment of choice. However, recurrence is likely if the source of the trauma is not removed. Surgical removal is also indicated for denture-induced fibrous hyperplasia. In addition, a new, better-fitting denture should be constructed, and the patient should be advised concerning correct methods of denture care. The prognosis for both forms of this lesion is excellent if the source of the irritation is removed. If the source is not eliminated, there is a good risk of recurrence.

Cowden syndrome (multiple hamartoma syndrome)

Cowden syndrome is an autosomal dominant **syndrome** (a group of symptoms associated with a certain disease/disorder) characterized by a variety of systemic, cutaneous, and oral manifestations. This is a rare disorder; however, since it has severe health implications, a discussion of the basic manifestations is appropriate. Almost all of the individuals affected by this genetic disorder develop facial papules, small 1- to 5-mm, flat-topped, flesh-colored growths. Many also have similar lesions on the hands and feet. Some 80% of patients also exhibit oral papules that are 1 to 3 mm in size, smooth-surfaced, and about the same color, or a little lighter than, the surrounding tissues. The oral lesions are histologically the same as fibromas. The most notable systemic manifestations include thyroid cancer and breast cancer. Approximately 7% of patients will have a thyroid malignancy and 20 to 36% of women will be diagnosed with breast cancer (Adkisson & Fiala, 2010). Men with this disorder also have a higher risk of breast cancer. These cancers do not develop until the individual is an adult, and the dental professional may be the first health care provider to discover the cutaneous and oral manifestations, which are rather nonspecific. Therefore, the clinician should suspect this disorder if multiple fibroma-like lesions are present and should make an appropriate medical referral. In addition, these patients should be monitored closely for the development of thyroid, breast, and other cancers.

NAME: Peripheral ossifying fibroma

Etiology: **Peripheral fibroma** is a reactive hyperplastic lesion that appears exclusively on the gingiva and is thought to originate from submucosal connective tissue or the periodontal ligament.

Method of Transmission: Not applicable

Epidemiology: This is a common oral lesion that occurs in both genders and at any age.

Pathogenesis: In most cases, a local factor such as calculus or some other type of foreign body initiates the hyperplastic process.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: Peripheral ossifying fibroma presents as a well-defined, firm, pedunculated or sessile, exophytic mass on the attached gingiva. It is usually smooth-surfaced and covered with normal mucosa, but it may have a rougher or papillary surface texture instead. These lesions are usually less than 1 cm in size. Lesions have a tendency to become traumatized the larger they get, so at times, the surface may be ulcerated. Most peripheral ossifying fibromas are located in interdental papilla areas (Figs. 17.5 and 17.6).

Distinguishing Characteristics: The peripheral ossifying fibroma is found exclusively on the attached gingiva.

FIGURE 17.5. Peripheral fibroma. Note the papillary surface texture of this peripheral fibroma. The color of this lesion is darker than normal, making this peripheral fibroma look very similar to a pyogenic granuloma.

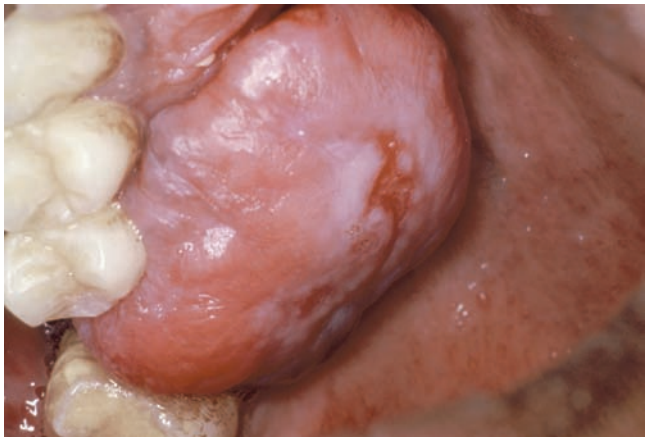

FIGURE 17.6. Peripheral ossifying fibroma. This exophytic growth arises from the attached gingiva. Note the ulcerated surface. (Courtesy of Dr. Michael Brennan.)

Significant Microscopic Features:

- The peripheral ossifying fibroma contains bone and deposits of cementum within an excessive collagenized connective tissue containing spindle-shaped fibrohistiocyte cells and variable amounts of inflammatory cells.
- The giant cell fibroma contains many multinucleated fibroblasts.
- The peripheral odontogenic fibroma is distinguished by the presence of odontogenic epithelium within the connective tissue.

The three subtypes cannot be differentiated on a clinical basis, and a biopsy is necessary for a definitive diagnosis.

Dental Implications: The peripheral ossifying fibroma is a reactive lesion; thus, it is important to try to identify the source of irritation or trauma and eliminate it.

Differential Diagnosis: Other soft tissue enlargements that form on the attached gingiva are included in the differential diagnosis. These include the following:

1. Pyogenic granuloma, Chapter 13
2. Peripheral giant cell granuloma, Chapter 13
3. Fibroma, Chapter 17
4. Traumatic neuroma, Chapter 17

Treatment and Prognosis: This lesion is treated by local excision with no recurrence usually expected. The prognosis is good if the underlying local factors are removed.

NAME: Generalized gingival hyperplasia

Etiology: Generalized gingival hyperplasia is a generic term used to describe an overgrowth of gingival tissues caused by a number of diverse factors. The most common cause of hyperplastic gingiva is an exuberant response to chronic inflammation associated with dental biofilm or other local factors such as calculus. Some cases of gingival hyperplasia are associated with specific drugs, notably the anticonvulsant *phenytoin* (used in the treatment of epilepsy), *calcium channel blockers* (used for treating cardiovascular conditions), and *cyclosporine* (used as an immunosuppressant in patients who have had organ or tissue transplants). Hormone changes in puberty and pregnancy have also been associated with an overgrowth of gingival tissues due to an exaggerated response to local factors, specifically, dental biofilm. Two other etiologic factors associated with this condition are discussed in previous chapters (Leukemia, Chapter 9, and Inherited traits, Chapter 6); both may cause generalized gingival enlargement. Information on these two etiologic factors is not repeated in this chapter. Refer to Chapters 6 and 9 for a review of this information.

Method of Transmission: Not applicable

Epidemiology: Gingival hyperplasia associated with medications is estimated to occur in 50% of those taking phenytoin, 27% of those taking cyclosporine, and 10 to 20% of those taking calcium channel blockers. There are no epidemiologic data available regarding hyperplasia related to hormone fluctuations or dental biofilm infections. There is equal distribution among ages, between genders, and across racial groups.

Pathogenesis: The mechanism that causes drug-induced and hormone-related gingival hyperplasia is not known. Some individuals may be more susceptible to the condition than others, and it is thought that this may be related to the presence of excessive amounts of keratinocyte growth factor, a type of fibroblast growth factor. Whatever the mechanism, poor oral hygiene plays a significant role in the development of gingival hyperplasia. Individuals who have inadequate oral hygiene and are taking drugs associated with this condition, or who are going through hormonal changes, have a higher risk of developing this condition than individuals who have good oral hygiene.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: The hyperplasia can be generalized or it can be limited to a localized area. It can range in severity from mild enlargement of the interdental papilla to being so severe it covers most of the coronal surfaces of the teeth. Hyperplasia associated with hormonal changes is usually more inflammatory and presents with edema and erythema. Drug-induced hyperplasia is often more fibrotic and presents as firm enlargement of the gingival tissues (Fig. 17.7). If oral hygiene is inadequate, the tissues appear inflamed and edematous in either case.

Distinguishing Characteristics: The clinical appearance of generalized gingival hyperplasia, coupled with a history of taking specific drugs or hormonal changes, distinguishes this condition from others.

Significant Microscopic Features: Excess amounts of fibrous connective tissue are seen, with or without inflammation.

Dental Implications: The clinician should obtain a thorough medical history and identify risk factors associated with

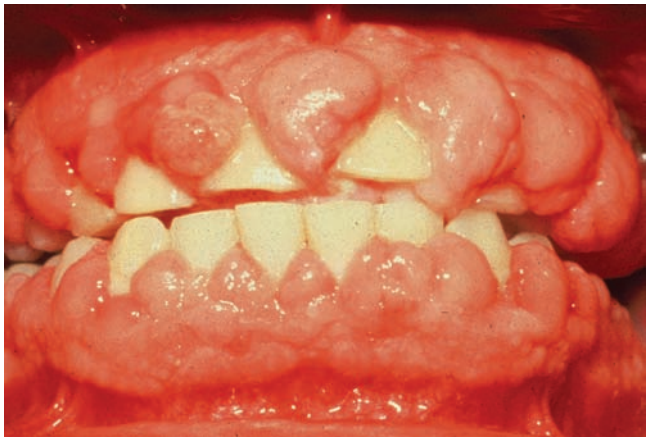

FIGURE 17.7. Generalized drug-induced gingival hyperplasia. In this case, the hyperplastic process is associated with the drug cyclosporine. (Courtesy of Dr. Terry Rees.)

this condition. Dental biofilm is associated with exacerbation of this condition, so patient instruction in oral hygiene is crucial, because it is much easier to prevent this condition than to treat it once it is established.

Differential Diagnosis: No differential diagnosis is necessary because this is a descriptive term; however, the cause of the hyperplasia must be determined. Some etiologic agents that should be considered in addition to hormones and drugs include the following:

1. Leukemia, Chapter 9
2. Dental biofilm infections (periodontitis or gingivitis)
3. Hereditary gingival fibromatosis, Chapter 6

Treatment and Prognosis: Discontinuance of the offending drug, especially cyclosporine, often results in reduction or resolution of the hyperplasia (Fig. 17.8). Increased efforts toward oral hygiene that result in the reduction of biofilm will reduce the inflammatory component of the hyperplasia. Surgical removal of the excess tissue, called **gingivectomy**, may be required when there is little or no resolution of the condition after oral hygiene has improved. The prognosis depends on the cause of the hyperplasia. Hormone-induced hyperplasia may resolve when hormones come back into balance. Drug-induced hyperplasia may resolve after discontinuing the drug. However, discontinuing the drug might not be an option, in which case there is a high probability that the hyperplasia will recur, even after surgical removal.

FIGURE 17.8. Generalized gingival hyperplasia. Same patient as in Figure 17.7 after discontinuing medication, showing resolution of the hyperplasia. (Courtesy of Dr. Terry Rees.)

NAME: Lymphoid hyperplasia

Etiology: **Lymphoid hyperplasia** (proliferation of lymph cells within lymph tissues) is a reactive response of the immune system caused by infectious agents or foreign substances that invade the body.

Method of Transmission: The infectious agents are transmitted according to their individual characteristics. The hyperplastic response is not transmissible but is specific for the individual host and depends on the status of the host's immune system and other individual traits.

Epidemiology: This lesion is found in patients of all ages and both sexes.

Pathogenesis: Lymphoid tissue is involved in both the identification and processing of viruses, bacteria, and other invaders of the host. Lymphoid hyperplasia increases the chance that the host will be able to defeat invading agents by providing more cells to destroy them. Acute infections, such as human immunodeficiency virus (HIV), may cause lymphoid tissues to respond very aggressively. The lingual tonsil seen in Figure 17.9 is elevated and appears very prominent in this patient.

Extraoral Characteristics: Lymphadenopathy is the abnormal enlargement of lymph nodes anywhere in the body.

Perioral and Intraoral Characteristics: Lymphoid tissue is abundant within the mouth (soft palate, hard palate, ventral surface of the tongue, and floor of the mouth) and is especially dense in Waldeyer ring (see Chapter 4). Lymphoid hyperplasia presents clinically with varying enlargements

FIGURE 17.9. Lymphoid hyperplasia. Lingual tonsil lymphoid tissue. (Courtesy of Dr. John Wright.)

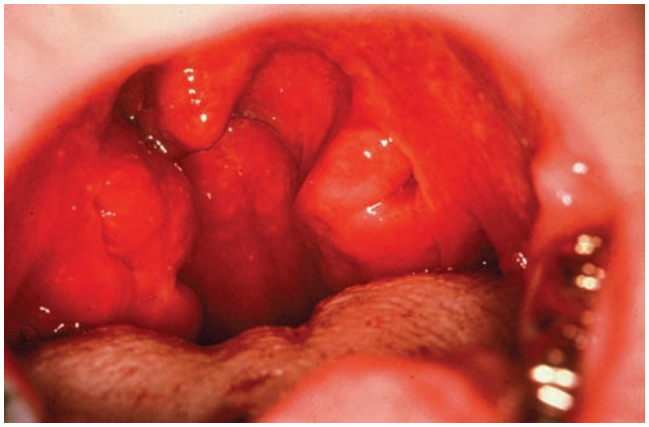

FIGURE 17.10. Lymphoid hyperplasia. Note the asymmetrical enlargement of the tonsils associated with lymphoid hyperplasia. (Courtesy of Dr. Michael Brennan.)

of the lymphoid tissue, which may appear bulbous, have a papillary or smooth surface, and in most cases are the same color or slightly lighter than the surrounding tissue. Hyperplasia may involve the lymphoid tissue in the tonsillar region, which may result in bulbous, enlarged tonsils (Fig. 17.10), or it may occur in the posterior portion of the lateral border of the tongue mixed with the **foliate papilla** (folds of tissue containing taste buds that are located on the posterior lateral border of the tongue). When hyperplasia occurs in this area, it can become traumatized and appear very suspicious for oral cancer, which is common at this site as well.

Distinguishing Characteristics: The location of the hyperplastic tissue in areas associated with lymphoid tissue suggests lymphoid hyperplasia, but other entities should be ruled out.

Significant Microscopic Features: Proliferation of lymphocytes is evident as well as the presence of numerous macrophages.

Dental Implications: Identification of the hyperplastic tissue is important to rule out more serious conditions such as cancer. The tonsillar region should always be included in the oral cancer examination. This region is often neglected and believed to be beyond the dental practitioner's area of expertise. Any abnormality that is observed should be followed with further evaluations on a periodic basis. In addition, patients may need to be referred to a physician for evaluation for systemic conditions such as infections.

Differential Diagnosis: Any of the disorders that could present as enlargement of lymphoid tissue, or look similar to this, need to be ruled out. Some of these include the following:

1. Carcinoma, Chapter 5
2. Lymphoma, Chapter 9
3. Fibroma and denture-induced fibrous hyperplasia, Chapter 17

Treatment and Prognosis: Treatment is not necessary unless the tissue becomes large enough to impede oral functions such as eating or is chronically traumatized. The prognosis is good. Biopsy may be needed to distinguish what appears to be a hyperplastic malignancy.

NAME: Sarcoidosis

Etiology: **Sarcoidosis** is a multisystem inflammatory disease of unknown etiology that results in the formation of granulomas within affected organs and tissues. Current research supports evidence that this is neither a neoplastic nor an autoimmune disorder. In addition, pathogenic organisms have not been consistently associated with sarcoidosis, although **mycobacteria** (gram-positive, aerobic, nonmotile rods) and Epstein-Barr virus have been suggested. There is some evidence that both genetic and environmental factors play a role in the development of sarcoidosis. Recent studies indicate that World Trade Center responders exposed to environmental agents may show "sarcoid-like" granulomas from exposure to environmental agents and foreign antigens (Crowley et al., 2011; Newman & Newman, 2012). Areas that are contaminated with mold or mycobacteria are also being evaluated as agents capable of promoting a hypersensitivity immune response. The evidence appears to suggest that there may be multiple triggers.

Method of Transmission: It is unknown whether or not this disease is transmissible; however, most believe that it is not passed from person to person.

Epidemiology: Five to forty of every 100,000 individuals are estimated to be affected by this disease. The prevalence is higher in blacks than in whites, and females are affected more often than males. The incidence of sarcoidosis peaks between the ages of 25 and 35 years. Females experience a second peak between 45 and 65 years of age.

Pathogenesis: Sarcoidosis is characterized by an exaggerated immune response to an unknown antigen or antigens within the organs that are affected. Lymphocytes, macrophages, mast cells, and natural killer cells perpetuate the immune response and cause a chronic inflammatory process that results in the formation of granulomas. See Chapter 3 for a review of the chronic inflammatory process.

Extraoral Characteristics: Sarcoidosis can affect any organ, but the respiratory system is the main target. Respiratory manifestations include shortness of breath and a persistent cough. Progressive disease can result in respiratory failure. Ocular involvement can cause cataracts, glaucoma, or blindness. Dermatologic manifestations include a maculopapular rash (rash consisting of raised papules surrounded by flat areas of erythema) that can occur on the limbs, face, and buttocks (Fig. 17.11). In addition, painful inflammation of subcutaneous adipose tissues *(erythema nodosum)* may be seen on the arms and the legs, especially on the shins. Granulomas are often found in the liver but usually are not associated with abnormal liver function.

FIGURE 17.11. Sarcoidosis. Maculopapular rash on the face of an individual who has sarcoidosis. (From Goodheart HP. Goodheart's photoguide of common skin disorders. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

Perioral and Intraoral Characteristics: Salivary gland enlargement, especially of the parotid gland, and xerostomia are possible in sarcoidosis. Other oral lesions present as either firm or spongy papular or nodular growths found on the gingiva, lips, palate, buccal mucosa, or tongue (Fig. 17.12).

Distinguishing Features: Not applicable

Significant Microscopic Features: Granulomas surrounded by an intense infiltrate of lymphocytes and multinucleated foreign body giant cells are characteristic of sarcoidosis.

Dental Implications: The patient should be encouraged to adhere to a good oral hygiene regimen because of the potential for involvement of the gingival tissues. If xerostomia is present, the patient should be counseled on how to manage the associated symptoms (see Clinical Protocol #4).

Differential Diagnosis: Any other condition associated with parotid gland enlargement needs to be considered, including the following:

1. Papillary cystadenoma lymphomatosum, Chapter 17
2. Alcoholism. Chronic alcoholism can cause a diffuse parotid gland enlargement similar to that seen in sarcoidosis. A careful personal/medical and dental history might give the clinician clues as to whether this is a consideration.
3. Diabetes, Chapter 7
4. Eating disorders. Patients with eating disorders may exhibit parotid gland enlargement. The presence of other signs and symptoms of eating disorders, such as enamel erosion, would help to suggest this diagnosis.
5. Salivary neoplasms, Chapter 17
6. Sjögren syndrome, Chapter 17

In addition, oral mucosal lesions associated with sarcoidosis may resemble those seen in Crohn disease (see Chapter 10) and some deep fungal infections (see Chapter 12).

Treatment and Prognosis: Patients often experience spontaneous resolution of the disease. Many other patients live a long productive life with few if any symptoms or manifestations. Still others experience intermittent exacerbations of the disease and require treatment with corticosteroids. These patients must be evaluated for disease manifestations by a physician on a regular basis. Topical steroids may help manage oral lesions. The prognosis is good for those affected by sarcoidosis. Death due to sarcoidosis occurs in less than 5% of untreated patients and is usually associated with respiratory failure or right heart failure.

Ranula

Ranula is a descriptive term used to describe a swelling in the floor of the mouth that resembles a frog's belly (Fig. 17.13). The term usually refers to a swelling that is caused by obstruction of the submandibular or sublingual salivary glands, which results in the development of an inflammatory response. In this case, the ranula is the clinical manifestation

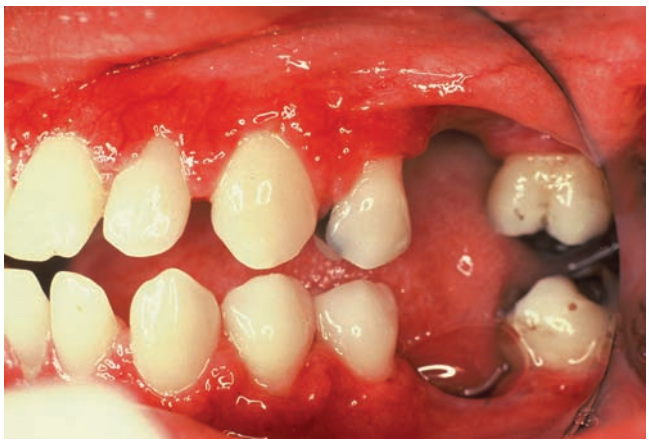

FIGURE 17.12. Sarcoidosis. Note the small papular growths on the free and attached gingiva in this individual. (Courtesy of Dr. Terry Rees.)

FIGURE 17.13. Ranula. (Courtesy of Dr. Shabnum Meer.)

of a mucocele that is seen in the floor of the mouth (see Chapter 11). Obstruction of the duct can be associated with trauma or with a sialolith (salivary duct stone). If the lesion herniates through the mylohyoid muscle, it is called a "plunging ranula" and appears in the area of the neck.

Confusion may occur with mucoceles and enlargements on the ventral tongue region. Some salivary gland tissue is found in this region, called the **glands of Blandin-Nuhn.** This growth emanates from the mixed mucous and serous glands that are imbedded within the musculature of the anterior tongue. The glands are neither lobulated nor encapsulated. These glands drain by means of five to six small ducts that open near the lingual frenum. This is the second most commonly occurring mucocele, although 70% of mucoceles occur in the minor salivary glands of the lip. The growth may appear circumscribed, somewhat fluid but firm, with a blue-to-reddish color. The growth is surgically removed. The differential diagnosis of the lymphangioma (discussed later in this chapter) should be considered as well.

Infections

Oral infections can cause soft tissue enlargements. Edema from the inflammatory process can affect any of the oral tissues. This section focuses on infections that cause enlargement of the salivary glands. The parotid gland is affected more often than the other major glands. Parotid enlargement may be clinically visible when the clinician stands in front of the patient and assesses facial symmetry and fullness. The patient may also report feelings of pressure and a sense of fullness.

NAME: Mumps (viral sialadenitis)

Etiology: Mumps is caused by a Paramyxovirus.

Method of Transmission: Mumps is transmitted by direct contact with the saliva or saliva droplets of an infected person.

Epidemiology: In 1964, more than 200,000 cases of mumps were reported. This number dropped dramatically with the introduction of a vaccination against the virus that causes mumps. In 2003, only 231 cases were reported across the United States (Defendi et al., 2012). Periodic outbreaks occur in isolated areas of the United States and also in other countries. In January 2010, the CDC reported an outbreak of 1,521 cases of mumps in a religious community. Over 88% of those affected had received at least one dose of vaccine (and 75% of these had received two doses), showing that, even with the vaccine, pockets of the disease can still occur.

Pathogenesis: Mumps has an incubation period of 14 to 25 days; then nonspecific symptoms of low-grade fever, malaise, headache, and chills occur and last anywhere from 3 to 5 days. After this, the patient may experience swelling of the salivary glands. The most common presentation is a **parotitis** (inflammation of the parotid gland), which occurs in 30 to 40% of patients. Other reported sites of infection are the testes, pancreas, eyes, ovaries, central nervous system, joints, and kidneys. A patient is considered infectious from about 3 days before the onset and up to 4 days into active parotitis. Infections can be asymptomatic in up to 20% of persons.

Extraoral Characteristics: In addition to the general systemic manifestations of the infection, specific complications can occur. This virus can potentially affect any glandular tissue within the body. Some of the tissues that may be affected include the liver, pancreas, kidney, and nervous system. Encephalitis is a rare complication, but it accounts for the 1.4% mortality rate associated with the disease. The sex organs, testes and ovaries, can also be affected if the infection occurs postpuberty. **Orchitis** is the term used to describe inflammation of the testes, and **oophoritis** describes inflammation of the ovaries. Rarely, male sterility can result from this type of inflammation.

Perioral and Intraoral Characteristics: Swelling can occur in any of the major salivary glands, but the parotid gland is affected more often than the others (Fig. 17.14). The classic presentation in the parotid gland includes swelling that lifts the ear lobe upward and outward. There may be erythema surrounding the salivary ducts (Wharton and/or Stensen ducts). The patient may complain of pain when chewing or when eating foods that stimulate the salivary glands. Pain may also occur in and around the ear because of pressure from the swelling.

Distinguishing Characteristics: The presence of swelling of the salivary glands, in addition to the systemic manifestations associated with viral infections, strongly suggests this condition.

Significant Microscopic Features: The mumps virus can be isolated from urine, blood, and nasopharyngeal and buccal swabs for up to 7 days before and 9 days following the appearance of salivary gland swelling.

FIGURE 17.14. Mumps. A unilateral swelling of the parotid gland is clinically evident in this child who has mumps. (From Fleisher GR, Ludwig W, Baskin MN. Atlas of pediatric emergency medicine. Philadelphia: Lippincott Williams & Wilkins, 2004.)

Dental Implications: It is important to recognize the manifestations of this infection so that the patient can be referred for medical evaluation.

Differential Diagnosis: No differential diagnosis is necessary, as mumps is easily diagnosed from the symptoms and a history of exposure to the virus.

Treatment and Prognosis: Treatment is focused on relieving the general symptoms associated with a viral infection and includes bed rest, plenty of fluids, and analgesics for pain and fever. The prognosis is excellent, and most individuals recover completely. Rarely, the infection results in the complications noted above.

NAME: Bacterial sialadenitis

Etiology: Pathogens that have been associated with **bacterial sialadenitis** include *Staphylococcus aureus, Streptococcus viridans, Streptococcus pneumoniae,* and *Haemophilus influenzae,* among others.

Epidemiology: This infection tends to appear in older, debilitated patients because this population group has more of the risk factors than any other age group.

Method of Transmission: This infection is not transmitted from person to person.

Pathogenesis: Bacterial sialadenitis develops from an overgrowth of bacteria in a gland that is not producing adequate amounts of saliva (xerostomia) to keep the bacterial population under control. The overgrowth of bacteria causes acinar and ductal inflammation and can lead to the destruction of these cells over time. The xerostomia that predisposes an individual to this infection is often related to medications, connective tissue disorders that include Sjögren syndrome as a component, postradiation therapy side effects, side effects related to salivary gland surgery, and inadequate hydration.

Extraoral Characteristics: Systemic manifestations of fever, malaise, and headache are often present.

Perioral and Intraoral Characteristics: Painful swelling of the affected gland is the classic clinical feature of this infection. **Trismus** (persistent contraction of the masseter muscle) is common, as is painful chewing. Purulent exudate may be present at the duct orifice, and exudate may be expressed from the gland with gentle pressure.

Distinguishing Characteristics: Inflammation of the salivary ducts and the presence of purulent exudate are characteristic of this infection.

Significant Microscopic Features: Not applicable

Dental Implications: Xerostomia is one of the major risk factors for developing this infection. Patients who have xerostomia should be monitored closely. In addition, they should be educated about various strategies that can be used to alleviate xerostomia. (See Clinical Protocol #4 for additional information.)

Differential Diagnosis: The characteristic features of this infection make a differential diagnosis unnecessary.

Treatment and Prognosis: This infection may be difficult to treat. The exudate coming from the gland should be cultured to determine the specific bacteria responsible, so that the appropriate antibiotic can be prescribed. Analgesics are used to help decrease pain, and moist compresses, rehydration, and stimulation of salivary flow are helpful in alleviating discomfort. The prognosis is good in most cases. Occasionally, the infection may extend into the tissues surrounding the gland and cause spread of the infection into the neck or ear.

Immune System Disorders

Parotid enlargement can result from an immune system disorder. Many connective tissue disorders associated with immune system dysfunction include salivary gland dysfunction, with or without enlargement, as one of their elements.

NAME: Sjögren syndrome

Etiology: **Sjögren syndrome** is an autoimmune disorder.

Method of Transmission: Not applicable

Epidemiology: Sjögren syndrome is the second most common connective tissue disorder after lupus erythematosus. It affects about 3% of the population. About 90% of patients with Sjögren syndrome are women between the ages of 30 and 65 years. Approximately 4,000,000 Americans live with the disease. The Sjogren's Syndrome Foundation is an excellent resource for patients and families.

Pathogenesis: The destruction of the exocrine glands, especially the salivary and lacrimal glands, is caused by activated T cells that infiltrate the glands (for reasons that are not clear) and attack the acinar cells and the gland ducts. The presence of the large numbers of T cells causes glandular enlargement, and destruction of the acini causes loss of function. There are two forms of the disease, primary and secondary. *Primary Sjögren syndrome* occurs as isolated destruction of the lacrimal and salivary glands, while *secondary Sjögren syndrome* occurs in conjunction with another autoimmune disorder. The most common associated disorder is rheumatoid arthritis (see Chapter 10); others include systemic lupus erythematosus (see Chapter 12) and scleroderma (see Chapter 23). Recent articles by M.P. Pender (2012) suggest that many of the autoimmune-type diseases may be associated with $CD8^+$ T-cell deficiency, Epstein-Barr virus infection, vitamin D deficiency, and increases in these types of disease states. Further evaluation and studies need to be pursued.

Extraoral Characteristics: Changes in the lacrimal gland cause **keratoconjunctivitis sicca** (**xerophthalmia** or "dry eyes"), which is associated with blurring of vision, burning, and itching. Most patients complain of severe

photophobia (sensitivity to light) and a feeling that there is something in their eyes. If this condition is not managed correctly, the cornea can become eroded and ulcerated, and permanent damage can result. While the salivary and lacrimal glands are affected most often, any mucosal surface is at risk. This has implications within the intestinal, respiratory, and genitourinary tracts. Pulmonary disease and frequent infections often manifest when the mucus-producing cells of the bronchi are involved. The mucus becomes very thick and sticky and is more prone to colonization by pathogenic bacteria. Gastrointestinal (GI) problems might include dysphagia (difficult or painful swallowing) and inflammation of the mucosal surfaces of the GI tract due to inadequate and abnormal secretions. Liver disease, kidney disease, and inflammation of the thyroid have all been reported with Sjögren syndrome. Secondary Sjögren syndrome presents identically but with the additional manifestations of the concurrent connective tissue disorder.

Perioral and Intraoral Characteristics: The most significant oral manifestation of Sjögren syndrome is xerostomia, which varies in severity from individual to individual. Patients complain of difficulty swallowing, altered taste, and difficulty wearing prosthetic devices such as dentures. Xerostomia may cause the oral tissues to atrophy and the tongue to become more fissured. The parotid glands and/or the submandibular glands become enlarged in about 50% of patients with this disorder. The enlargement is usually bilateral and symmetrical and may recur and regress many times over the course of the disease (Fig. 17.15).

FIGURE 17.15. Sjögren syndrome. This patient had bilateral swelling of the parotid glands associated with Sjögren syndrome. Note the redness surrounding the eyes, which indicates keratoconjunctivitis sicca.

Distinguishing Characteristics: The most common clinical presentation of secondary Sjögren syndrome is a triad manifestation of rheumatoid arthritis, xerostomia, and keratoconjunctivitis.

Significant Microscopic Features: Heavy lymphocyte infiltration that replaces major salivary gland tissue is characteristic of Sjögren syndrome.

Dental Implications: Xerostomia increases the patient's risk for dental caries, periodontal disease, and infections such as candidiasis (see Chapters 13 and 14). Refer to Clinical Protocol #4 for more information on the management of xerostomia. These patients should be periodically monitored for neoplastic changes in the parotid gland (see below).

Differential Diagnosis: The differential diagnosis of a diffuse parotid enlargement includes the following conditions:

1. Papillary cystadenoma lymphomatosum, Chapter 17
2. Alcoholism. Chronic alcoholism can cause a diffuse parotid gland enlargement similar to that seen in Sjögren syndrome. A careful personal/medical and dental history might give the clinician clues about whether this is a consideration.
3. Diabetes, Chapter 7
4. Eating disorders. Patients with eating disorders may exhibit parotid gland enlargement. The presence of other signs and symptoms of eating disorders such as enamel erosion would suggest this diagnosis.
5. Salivary neoplasms, Chapter 17

An assessment of salivary function, including, but not limited to, salivary flow rate of individual glands and of the oral cavity as a whole (stimulated and unstimulated) is the mode of assessment used most often. Biopsy of labial minor salivary glands, or sometimes the parotid gland, is often done to demonstrate lymphocyte infiltration. There are also blood tests that measure specific levels of autoantibodies particular to several of the autoimmune diseases, including Sjögren syndrome, which can help to create a more definitive diagnosis.

Treatment and Prognosis: Sjögren syndrome is usually treated by managing the symptoms of the disease. This includes the use of artificial saliva and tears, the extensive use of fluoride for caries prevention, and home care and diet modifications. Using fluoride varnish at every 3-month maintenance appointment is an excellent therapy for the Sjögren patient. Eye drops that are over the counter for dry eyes are beneficial for most patients (see Clinical Protocol #4). Another simple modification is the introduction of **xylitol** (an artificial sweetener)—sweetened chewing gum. Chewing gum physically stimulates saliva production, and the xylitol itself stimulates saliva production. Bacteria ingest xylitol over sucrose, but they are unable to metabolize it, so the number of bacteria and the level of acid in the mouth drop. Research on drugs that stimulate saliva production shows mixed results. When drugs are used, they should be used

with caution, and their effectiveness should be monitored. Over-the-counter eye drops for dry eyes are beneficial for most patients. Other products such as Lacisert and Restasis are marketed for dry eyes. Sjögren syndrome is a chronic condition that requires long-term management and lifestyle adaptations. The prognosis is normally good with strict adherence to modifications. The prognosis is complicated by the fact that about 6 to 10% of cases are associated with a malignant transformation of the altered glandular tissue to lymphoma. The Sjogren's Syndrome Foundation provides a list of clinical trials that are being conducted world wide.

Soft Tissue Neoplasms

Neoplastic soft tissue enlargements are often associated with specific gene mutations that may be inherited or created by environmental factors. Soft tissue neoplasms can be either benign or malignant. Benign neoplastic growths are usually well circumscribed and often *encapsulated* (surrounded by a fibrous tissue capsule). These may invade local tissues, but they are not able to metastasize. Malignant soft tissue growths invade local tissues and can metastasize to any part of the body. Malignant cells replace the normal functioning cells of an organ or tissue and can result in the death of the individual. Benign and malignant soft tissue neoplasms are derived from one or more of the tissues found in the body. Chapter 5 discusses the general characteristics of neoplastic growths. Table 5.2 lists the nomenclature for both benign and malignant neoplasms and may be referred to for review of this information.

NAME: Fibromatosis (desmoid tumor)

Etiology: **Fibromatosis** has no known etiology. There is no specific etiology associated with most of these types of neoplasms. They may be associated with mutation of the cell's DNA or disruption of another defense mechanism against uncontrolled growth of cells. At one time, they were thought to be reactive lesions, because they occasionally appeared at a site where a previous surgical procedure was performed.

Method of Transmission: Several forms of fibromatosis (myofibromatosis, familial adenomatous polyposis, and multicentric fibromatosis) are considered inherited conditions.

Epidemiology: These neoplasms are more frequent in those under the age of 40, with children and young adults affected most often. Females are more likely to have aggressive fibromatosis than males.

Pathogenesis: Fibromatosis represents a group of lesions that exhibit a somewhat aggressive behavior. They are more destructive than benign neoplasms but have no ability to metastasize.

Extraoral Characteristics: These growths can occur in any area of the body. In the head and neck area, these lesions appear as enlarging masses that are firm to palpation when found in soft tissues. They may also be found centrally located within bone, where expansion of the cortical bone may be observed.

FIGURE 17.16. Fibromatosis. This palatal lesion is an example of an aggressive fibromatosis. (Courtesy of Dr. John Jacoway.)

Perioral and Intraoral Characteristics: Fibromatosis manifests as a slowly enlarging soft tissue mass when observed in the oral cavity (Fig. 17.16). Facial asymmetry can be expected as the lesions enlarge. The soft tissues surrounding the mandible are commonly affected. If the bone of the mandible is affected, the lesions appear as ill-defined radiolucencies. Expansion of the cortical bone may occur.

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Spindle-shaped cells growing in bundles are characteristic of fibromatosis.

Dental Implications: Early diagnosis of any enlarging mass is crucial to obtaining a favorable treatment outcome. The dental hygienist is in an excellent position to provide thorough examinations, which can identify abnormal growths when they are small.

Differential Diagnosis: Any of the soft tissue tumors would have to be ruled out by biopsy. Specifically, fibromatosis must be differentiated from fibrosarcoma. The differentiation between the two depends largely on tumor behavior and somewhat less on the histology of the lesion.

Treatment and Prognosis: The treatment of choice is aggressive surgical excision. Chemotherapeutic agents (anticancer drugs) are sometimes used in addition to the surgery because there is a high rate of recurrence with these tumors. The tumors have been known to regress spontaneously, but, in general, they have a recurrence rate of approximately 25% in the head and neck area. Deaths have been reported due to recurrence and locally aggressive invasion of vital tissues.

NAME: Fibrosarcoma

Etiology: The development of **fibrosarcoma** may be linked to previous radiation therapy and tissue trauma such as a burn injury.

Method of Transmission: Not applicable

Epidemiology: This rare neoplasm occurs more often in young adults and children and slightly more often in males.

Pathogenesis: Fibrosarcoma is a malignant tumor of fibroblasts that can occur in soft tissues or within bone. Fibrosarcoma is characterized by a proliferation of fibroblasts. It usually arises about 10 years after radiation therapy or about 30 years after a burn injury. The entity may be classified as low or high grade.

Extraoral Characteristics: The most common extraoral presentation of fibrosarcoma is in the thigh bone around the knee joint.

Perioral and Intraoral Characteristics: Most of these lesions present as gradually enlarging, painless masses. Ulceration of the surface, secondary to trauma, may occur as the lesion enlarges. With enlargement, the patient may complain of pain, swelling, paresthesia, and loosening of teeth.

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Proliferating spindle cells are arranged in a herringbone pattern, and mitotic figures are commonly observed.

Dental Implications: Early identification of enlarging soft tissue masses is of utmost importance in obtaining a favorable treatment outcome.

Differential Diagnosis: Any of the soft tissue tumors need to be ruled out by biopsy. The neoplasms most likely to be considered include the following:

1. Fibromatosis, Chapter 17
2. Leiomyosarcoma, Chapter 17
3. Melanoma, Chapters 5 and 15
4. Spindle cell carcinoma

Treatment and Prognosis: The treatment of choice is surgical excision with wide margins. The prognosis is guarded. There is local recurrence in 50 to 75% of cases, and this is the most common cause of death. Distant metastasis occurs in 20 to 40% of cases, with spread occurring more commonly to the lungs. The 5-year survival rate is 50 to 70%.

NAME: Neurilemoma (schwannoma)

Etiology: The **neurilemoma** arises from proliferation of the Schwann cells of the nerve sheath.

Method of Transmission: Not applicable

Epidemiology: Neurilemomas are found most often in individuals between the ages of 20 and 50 years. They present in the oral cavity in both genders in equal numbers.

Pathogenesis: This is a slow-growing tumor that can occur in soft tissues or within bone. As the Schwann cells proliferate, they become surrounded by a fibrous capsule. The nerve does not become entangled with the tumor but is pushed aside as the tumor grows.

FIGURE 17.17. Neurilemoma of the lip. The lip is not a common location in which to find this lesion. (Courtesy of Dr. Jacob Jacoway.)

Extraoral Characteristics: Neurilemomas usually appear as small, smooth-surfaced, firm, nodular growths in the head and neck area and on the flexor surfaces of the arms and legs. The lesions are normally painless unless they are very large or they impinge on vital tissues (Kao, 2012). One form, the acoustic neurilemoma, affects the eighth cranial nerve at about the position of the internal auditory meatus. These can cause tinnitus (ringing in the ears) and deafness.

Perioral and Intraoral Characteristics: Intraoral neurilemomas manifest as smooth-surfaced submucosal masses (Fig. 17.17). The lesions can occur anywhere in the mouth but occur most frequently on the tongue. They can also occur within the bone of the maxilla or mandible, where they appear as well-defined radiolucencies. Bone lesions are often associated with pain and paresthesia (numbness).

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: The neurilemoma is a mass of spindle-shaped cells surrounded by a fibrous capsule composed of residual nerve fibers and the connective tissue that forms the support structure for the peripheral nerves.

Dental Implications: Accurate interpretation of radiographic findings in areas where a patient reports pain and/or paresthesia may be essential to detect this neoplasm, when it arises in bone.

Differential Diagnosis: Any of the soft tissue tumors must be ruled out by biopsy. The most likely soft tissue growths that should be considered include the following:

1. Neurofibroma, Chapter 17
2. Leiomyoma, Chapter 17
3. Traumatic fibroma, Chapter 17
4. Lipoma, Chapter 17

Treatment and Prognosis: The treatment of choice is surgical excision. There is little chance of recurrence, and the prognosis is excellent.

NAME: Neurofibroma

Etiology: The solitary **neurofibroma** is a benign neoplasm that originates from the Schwann cells and/or

connective tissue cells that support the peripheral nerves. Neurofibromatosis *(von Recklinghausen disease of the skin)* is an inherited syndrome characterized by multiple neurofibromas and other abnormalities. The solitary form of neurofibroma and the form associated with the inherited syndrome display similar clinical and microscopic appearances. Neurofibromatosis is discussed later in this chapter with other genetic disorders.

Method of Transmission: Not applicable

Epidemiology: The average age for developing a solitary oral neurofibroma is 45 years. There is no predilection for any race or gender.

Pathogenesis: The solitary neurofibroma may be found on any nerve, where it presents as a slow-growing, painless mass.

Extraoral Characteristics: Solitary neurofibromas may affect skin, major nerve plexuses, and the gastrointestinal tract, among others. The cutaneous presentation is a soft, nodular, sessile, or pedunculated growth. They are usually small, ranging in size from a few millimeters to several centimeters.

Perioral and Intraoral Characteristics: Intraorally, the tumor manifests as a slow-growing, smooth-surfaced, asymptomatic mass. It is most commonly located on the tongue or buccal mucosa; however, it can be located at any intraoral site (Fig. 17.18). Occasionally, the tumor may be found within the bone of the maxilla or mandible, where it can cause extensive expansion and destruction of the bone.

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Neurofibromas are composed of spindle cells in a delicate connective tissue matrix. Neurofibromas may be diffuse, with no apparent margins, or they may be well circumscribed. Mast cells are usually found within the lesion.

Dental Implications: The presence of multiple neurofibromas may indicate a relatively common genetic disorder called neurofibromatosis. The dental hygienist may be in a unique position to detect these lesions and request referral of the patient for medical evaluation.

Differential Diagnosis: Any of the soft tissue enlargements must be ruled out, including the following:

1. Neurilemoma, Chapter 17
2. Leiomyoma, Chapter 17
3. Traumatic fibroma, Chapter 17
4. Lipoma, Chapter 17

In addition, in the case of diffuse lesions of the tongue, other causes of macroglossia such as amyloidosis (see Chapter 9, multiple myeloma) or lymphangioma (see Chapter 17) need to be ruled out.

Treatment and Prognosis: Surgical excision is the preferred treatment. Solitary neurofibromas have little chance of recurrence and thus have an excellent prognosis.

FIGURE 17.18. Neurofibroma. This neurofibroma of the gingiva has caused significant deformity. If this had been detected earlier, it might have been easily removed. The solitary lesions have little chance of recurring. (Courtesy of Dr. John Jacoway.)

Neoplasms of Smooth Muscle

The **leiomyoma** is a benign neoplasm of smooth muscle that is commonly found in the muscular layer of the gut and in the uterus. Rarely, leiomyomas are found in the oral cavity, where they present as a slow-growing, painless, smooth-surfaced mass that is usually less than 2 cm in diameter. They can be found in any intraoral site; however, the tongue, hard palate, and buccal mucosa are frequently involved. Figure 17.19 shows a leiomyoma of the labial mucosa. Surgical removal is the treatment of choice, and the chance of recurrence is negligible.

The leiomyosarcoma is a malignant neoplasm of smooth muscle that occurs most often in the deep tissues of the extremities and within the muscular layers of the esophagus. It occurs infrequently within the oral cavity, where the tissue of origin is the smooth muscle associated with the walls of blood vessels. The lesions usually manifest as painful masses in the jaws or gingival tissues. The treatment of choice is surgical excision with wide margins. Local recurrence of the tumor is seen in 30% of cases, and metastasis to the cervical lymph nodes or to the lungs is reported in more than 50% of cases. The long-term prognosis is poor.

FIGURE 17.19. Leiomyomas present as smooth-surfaced submucosal masses, such as this leiomyoma in the lip.

FIGURE 17.20. Rhabdomyoma. This is an example of a rhabdomyoma on the dorsal surface of the tongue. (Courtesy of Dr. Valerie A. Murrah.)

FIGURE 17.21. Periorbital rhabdomyosarcoma is a rapidly growing tumor seen most often in young children. (Courtesy of Dr. John Jacoway.)

Neoplasms of Striated Muscle Cells

The rhabdomyoma is a benign neoplastic growth of striated muscle cells. These tumors are very rare but tend to form in the soft tissues of the head and neck more frequently than in other areas. They appear as painless submucosal swellings of the floor of the mouth, tongue, and soft palate (Fig. 17.20). Surgical removal is the treatment of choice, and there is little chance of recurrence. The malignant counterpart of the rhabdomyoma is the rhabdomyosarcoma.

NAME: Rhabdomyosarcoma

Etiology: The **rhabdomyosarcoma** is a malignant tumor of striated muscle that has an unknown etiology. Several genetic syndromes, including neurofibromatosis and nevoid basal cell carcinoma syndrome, and several environmental agents, including intrauterine exposure to x-radiation, have been associated with an increased risk of developing this tumor. Some children with certain birth defects are at a higher risk and some families may have a gene mutation, placing them at higher risk.

Method of Transmission: Not applicable

Epidemiology: Rhabdomyosarcoma is the most common soft tissue sarcoma seen in children. Approximately 87% of cases are found in children under the age of 15 years. Some 250 cases, about 6 individuals out of 1 million, are diagnosed every year in the United States. The tumor occurs equally in all ethnic groups and is slightly more common in males.

Pathogenesis: Rhabdomyosarcoma presents as a rapidly growing mass. The lungs, bone, and bone marrow are the most common sites for metastasis.

Extraoral Characteristics: These tumors are found most often in the head and neck area, extremities, and the genitourinary tract. Symptoms are usually related to the location of the tumor. The growths may be palpable if superficially located. One of the most common sites of involvement in the head and neck is the orbital area (33% of cases) (Fig. 17.21). Deeper growths may not be discovered until they are very large and become symptomatic.

Perioral and Intraoral Characteristics: When this lesion develops intraorally, it is found on the hard and soft palates and the tongue more frequently than in other areas. Symptoms of pain and paresthesia may be present, especially if the jaw is involved. Lesions located within the jaws appear radiographically as ill-defined radiolucencies.

Distinguishing Characteristics: Rapidly growing soft tissue masses in the orbital region should alert the clinician to the possibility of rhabdomyosarcoma.

Significant Microscopic Features: There are three main histologic forms of this neoplasm, ranging from neoplasms with well-differentiated cells that exhibit the striations normally seen in striated muscle to oddly shaped cells that exhibit few if any striations.

Dental Implications: Any soft tissue enlargement that has not been identified and does not resolve over a 2-week period should be biopsied. Patients should have dental evaluations prior to starting chemotherapy and/or radiation therapy. Refer to Clinical Protocol #19 for a review of the procedures that need to be done prior to chemotherapy or radiation therapy.

Differential Diagnosis: Other tumors that manifest as rapidly growing enlargements need to be considered in a differential diagnosis. These include the following:

1. Myofibroma, Chapter 17
2. Ewing sarcoma, Chapter 18
3. Lymphoma, Chapter 9
4. Osteosarcoma, Chapter 18

Treatment and Prognosis: The standard treatment for rhabdomyosarcoma is complete surgical removal combined with chemotherapy and radiation therapy. The prognosis varies widely, according to the location of the tumor, its histologic characteristics, and whether there has been metastasis. The 5-year survival rate for localized disease is more than 80%, while that for metastatic disease is less than 30% (Cripe, 2011).

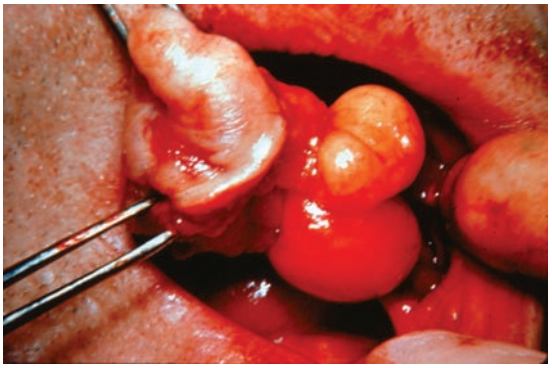

FIGURE 17.22. This lipoma is being excised from the buccal mucosa. The lipoma is the small, smooth-surfaced, yellowish mass to the right of center in the photograph.

Neoplasms of Fat Tissue

The lipoma is a benign neoplasm of adipose cells. This neoplasm is considered the most common soft tissue tumor in the body, and it can occur in any tissue or organ; however, it is rare in the oral cavity. Intraorally, lipoma appears as a superficial, smooth-surfaced, soft, palpable mass that often imparts a yellowish color to the overlying mucosa (Fig. 17.22). The buccal mucosa is the most common site followed by the tongue (Manor et al., 2011). The tumor may also affect the floor of the mouth. No sex predilection is noted (Manor et al., 2011). This lipoma is found more often in adults around the age of 50 years. Surgical removal is the treatment of choice, and recurrence is not a factor. The average size of most tumors is from 0.5 to 8.0 cm. Blunt force tissue trauma has been reported to occur in many cases prior to lipoma development.

The malignant counterpart of the lipoma is the liposarcoma. Like the lipoma, the liposarcoma is rarely found in the oral cavity. Surgical excision is the treatment of choice, and the prognosis is normally good; however, the tumor has a tendency to recur, and the prognosis becomes less favorable with each recurrence. These patients should be followed closely by a dental professional to facilitate the early discovery of any recurrent lesions.

Salivary Gland Neoplasms

Salivary gland tumors constitute a relatively uncommon, but important, set of soft tissue lesions. In addition to the major salivary glands (parotid, submandibular, and sublingual), hundreds of minor salivary glands exist throughout the oral mucosa. Salivary gland neoplasms, both benign and malignant, usually present as smooth-surfaced masses of the soft tissue; therefore, the role of palpation in the detection of these tumors and in their clinical characterization is paramount. If tumors arise in the major salivary glands, it is often necessary to remove the entire gland to remove the tumor. In the case of the parotid gland, the facial nerve may have to be sacrificed. Complications of facial nerve damage are identical or similar to those seen in Bell palsy (see Chapter 10). The dental hygienist may have to educate the patient about methods of managing the complications associated with facial nerve damage if present. Obviously, the earlier the tumor is discovered, the less facial damage may occur and the patient will suffer less trauma.

NAME: Pleomorphic adenoma (mixed tumor)

Etiology: The **pleomorphic adenoma** is a benign neoplasm that arises from the proliferation of two different types of salivary gland cells, ductal and **myoepithelial** (contractile cells of epithelial origin). Alterations in chromosome 8 may be associated with the development of this neoplasm.

Method of Transmission: Not applicable

Epidemiology: This is the most common benign salivary gland neoplasm, accounting for about 80% of these tumors. Pleomorphic adenoma or mixed tumors range from 53 to 57% of parotid tumors and 44 to 68% of submandibular tumors. They have been reported in all age groups but predominate in middle-aged individuals, from 30 to 50 years. Some rare cases have been reported in children (Arcuri et al., 2011). Most studies report a female predilection.

Pathogenesis: Pleomorphic adenomas typically arise as slow-growing, firm masses that are slightly compressible. Pleomorphic adenomas have a tendency to recur; in addition, there is a slight chance they will undergo malignant transformation (carcinoma ex pleomorphic adenoma).

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: This neoplastic growth affects the parotid gland more often than any of the other major salivary glands, but it is not uncommon to find it in any of the major glands. It may also be seen in the minor salivary gland tissue at times. It manifests as a painless, slow-growing, firm mass, usually found in the lower superficial lobe of the parotid near the angle of the mandible (Fig. 17.23). Within the oral cavity, the pleomorphic adenoma appears as a firm, nodular growth covered by intact mucosa, most often found on the palate (Fig. 17.24A),

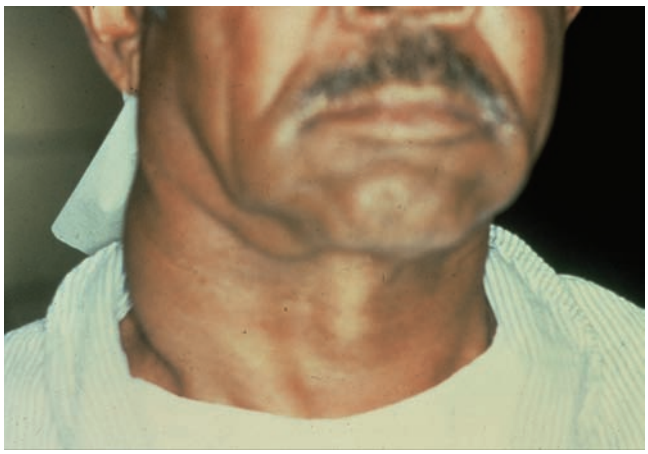

FIGURE 17.23. Pleomorphic adenoma presents as an enlargement of a salivary gland in the right neck region. The parotid gland is the gland most commonly involved. (Courtesy of Dr. Carolyn Bentley.)

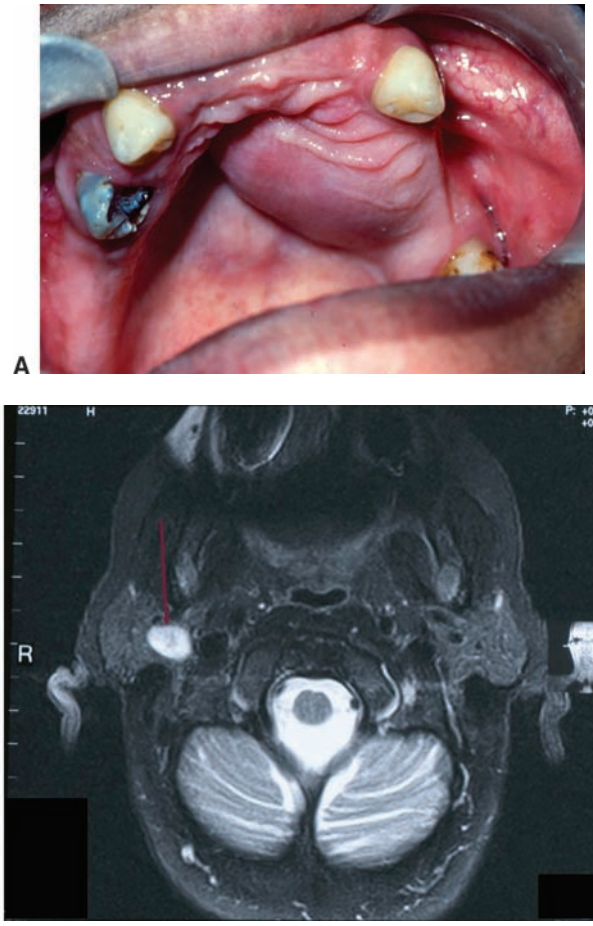

FIGURE 17.24. A. Pleomorphic adenoma. When this lesion is found intraorally, it is seen on the palate (as shown here) more than in any other area. **B.** Scan of a pleomorphic adenoma. The *arrow* points to the tumor.

followed by the upper lip and buccal mucosa. The tumors are mobile when found in the soft tissues but are not mobile when found on the palate.

Distinguishing Characteristics: Not applicable

Significant Microscopic and Radiographic Features: These tumors have a wide range of histologic presentations, with varying amounts of ductal versus myoepithelial cells and various patterns of growth. The term "pleomorphic" describes this wide variation in microscopic appearance. The pleomorphic adenoma is frequently surrounded by a capsule (encapsulated) that may have nests of neoplastic cells extending through it. This is thought to be the reason for its high recurrence rate. Figure 17.24B depicts the CT image of a pleomorphic adenoma. These neoplasms are not visible on conventional radiographs.

Dental Implications: Pleomorphic adenomas are difficult to remove completely; therefore, it is essential to monitor these patients periodically for recurrences.

Differential Diagnosis: Other salivary gland tumors must be ruled out; in addition, the following conditions should receive consideration:

1. Lymphoma, Chapter 9
2. Sarcoidosis, Chapter 17
3. Lymphadenopathy, mentioned in many chapters in association with many disorders
4. Peripheral nerve sheath tumors
5. Mucoepidermoid carcinoma
6. Metastatic disease states

Intraoral involvement of the minor salivary glands can mimic other soft tissue enlargements, and lesions such as the lipoma (see Chapter 17) and necrotizing sialometaplasia (see Chapter 12) should also be included in a differential diagnosis.

Treatment and Prognosis: Complete surgical removal is recommended, with enough adjacent tissue removed with the tumor to ensure that there are no remaining nests of cells. Excision of parotid tumors normally requires techniques that allow the facial nerve to be preserved. Tumors located on the palate may require the removal of some bone. The prognosis is excellent for pleomorphic adenomas that have been removed completely. Failure to adequately treat pleomorphic adenomas can result in significant morbidity due to extensive growth (Fig. 17.25) or in malignant transformation of the tumor. The likelihood of malignant transformation increases with the duration of the tumor, the number of recurrences, and the age of the patient.

Carcinoma Ex-Mixed Tumor

This rare malignant lesion develops within an already existing mixed tumor (pleomorphic adenoma). Most of these are found in the parotid gland (68%), while about 18% are found in the minor salivary glands. Surgical removal is the treatment of choice, but there is a 50% chance of recurrence. The 15-year survival rate is approximately 20%. Prompt identification and removal of pleomorphic adenomas drastically reduces the occurrence of these tumors.

Frey Syndrome

The parotid gland may have to be totally removed (parotidectomy) to obtain complete surgical excision of any neoplastic

FIGURE 17.25. Pleomorphic adenoma. When treated early, the prognosis for pleomorphic adenoma is excellent. However, failure to treat these neoplastic growths can result in extensive deformity as seen in this picture. (Courtesy of Dr. Robert J. Gorlin.)

growth in the gland. **Frey syndrome** is a common complication of this surgical procedure and represents a unique example of how nerve regeneration can go awry. In this case, the parasympathetic nerves that innervate the parotid gland are severed during the surgery, after which they may undergo abnormal regeneration and join with the sympathetic nerves that innervate the facial sweat glands. This abnormal regeneration causes about 50% of patients to report symptoms of facial sweating when their salivary glands are stimulated. In rare cases, the facial sweating can be copious; however, there are no serious problems associated with this condition. Medical therapies are available to manage Frey syndrome, for example, the use of local botulinum toxin (Botox) injections.

NAME: Papillary cystadenoma lymphomatosum (Warthin tumor)

Etiology: The etiology of these tumors is unknown, although multiple studies have shown a strong relationship of up to eight times the normal risk between smoking and the development of this tumor.

Method of Transmission: Not applicable

Epidemiology: **Warthin tumor** is the second most common benign parotid gland tumor. It usually appears in individuals between 40 and 70 years of age. The tumor is seen most often in white male smokers. Chedid (2011) noted a high rate of male smokers in a recent study of 70 cases.

Pathogenesis: The pathogenesis of Warthin tumor is largely unknown. The most accepted theory is that these tumors may originate from the entrapment of salivary gland cells within lymph nodes as the nodes are developing. Another possibility is that they develop from a proliferation of salivary gland tissue associated with lymphoid hyperplasia due to chronic inflammation. There is speculation that damage to mitochondrial DNA in the cells of the parotid gland may initiate the neoplastic process. The damage is thought to be associated with chemicals formed in the oral environment as a result of exposure to tobacco smoke when the tumor occurs in smokers.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: Warthin tumors present as slow-growing, rubbery or firm, painless masses, usually found in the tail of the parotid gland near the angle of the mandible (Fig. 17.26). There is a tendency for this tumor to appear bilaterally.

Distinguishing Characteristics: The tumors usually are bilateral. The patient may complain of tinnitus, pain in the ear, and deafness depending upon the stage of growth.

Significant Microscopic Features: The tumor is named for its microscopic appearance. Cystic spaces contain papillary projections that are lined by columnar cells, which are in turn supported by an underlying layer of lymphoid tissue.

Dental Implications: Patients who have a history of smoking have a much higher risk of developing this neoplasm.

FIGURE 17.26. Papillary cystadenoma lymphomatosum. Note the subtle swelling at the angle of the mandible where the tail of the parotid gland is located. This is the classic presentation of this tumor.

The dental professional should take this into consideration when performing extraoral and perioral palpations. In addition, since these tend to appear bilaterally, if one parotid gland is found to have a palpable mass, the opposite gland should be thoroughly palpated. The decrease in risk for this tumor can be mentioned as a benefit associated with smoking cessation.

Differential Diagnosis: Any of the salivary gland tumors that present as slow-growing masses or neoplasms that manifest as enlarged lymph nodes must be ruled out, including the following:

1. Pleomorphic adenoma, Chapter 17
2. Lymphoma, Chapter 9
3. Mucoepidermal carcinoma, Chapter 17

In addition, one should consider infectious diseases that manifest in the parotid gland, such as mumps, and metabolic conditions such as malnutrition (including malnutrition caused by eating disorders and chronic alcoholism) and diabetes mellitus in the differential diagnosis.

Treatment and Prognosis: Surgical removal of the tumor is the treatment of choice. A parotidectomy with a safety margin is the usual procedure. The prognosis is excellent. There is a chance of recurrence, but many feel that these recurrent tumors may actually be new primary lesions, especially if the patient has continued to smoke. There have been rare reports of malignant transformation within the tumors.

NAME: Mucoepidermoid carcinoma

Etiology: The etiology of **mucoepidermoid carcinoma** is not known.

Method of Transmission: Not applicable

Epidemiology: Mucoepidermoid carcinoma is the most common malignant salivary gland tumor in the United States. The highest numbers of cases occur in individuals during their second to seventh decade of life. This tumor is also considered the most common salivary gland malignancy in children. Slightly more females than males are affected.

Pathogenesis: The tumors are thought to arise from proliferation of undifferentiated excretory stem cells (stem cells involved with the development of the excretory duct system of the glands). The proliferation may be caused by inactivation of tumor suppressor genes or deletion of chromosomal material, among other possibilities.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: This malignant neoplasm is found most often in the parotid gland, where it manifests as an asymptomatic swelling. The lesion may exist for several years before it is reported by the patient or before it comes to the attention of a health care provider. The longer the tumor is present, the more likely that symptoms of pain and facial nerve paralysis or palsy will develop. Mucoepidermoid carcinoma may also affect the submandibular gland and the minor salivary glands found throughout the oral cavity. Minor salivary gland mucoepidermoid carcinomas appear as asymptomatic swellings, which may be fluctuant and slightly blue in color (Fig. 17.27). Mucoepidermoid carcinoma may also appear within the bone of the maxilla or more commonly the mandible, where it will present as a unilocular or multilocular radiolucency.

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Mucoepidermoid carcinoma is composed of a combination of mucus-secreting cells and epidermoid cells. These tumors exhibit varying degrees of aggressiveness from low grade to high grade, depending on their cellular composition. The more aggressive tumors have fewer mucus-secreting cells, while the less aggressive tumors have many mucus-secreting cells.

FIGURE 17.27. Note the bluish color of this palatal mucoepidermoid carcinoma. Significant amounts of underlying bone may have to be removed with this lesion if it is found to be a high-grade carcinoma.

Dental Implications: These tumors can be present for several years before they are noticed by the patient; therefore, oral cancer screening examinations should include palpation of all of the major salivary glands to identify abnormalities at an early stage.

Differential Diagnosis: The major entities in the differential diagnosis are other benign and malignant salivary gland tumors such as pleomorphic adenoma and polymorphus low-grade adenocarcinoma. In addition, an intraoral differential diagnosis includes the following:

1. Mucocele, Chapter 11
2. Neurofibroma, Chapter 17
3. Neurilemoma, Chapter 17
4. Lymphoma, Chapter 9

Treatment and Prognosis: This tumor is treated by surgical removal. The extent of the surgery depends on the size and grade of the tumor. Low-grade parotid tumors may require partial removal of the gland with the tumor, while saving the facial nerve. High-grade parotid tumors may require total removal of the gland and sacrifice of the facial nerve. Surgical removal of lesions affecting the minor salivary glands also depends on the tumor grade and can be conservative in low-grade lesions or can require the removal of large amounts of normal tissue, including underlying bone, in high-grade lesions. If there is evidence of metastasis, lymph nodes in the neck may have to be removed. Postsurgical radiation is often indicated as **adjuvant therapy** (additional treatment to enhance the primary therapy) for high-grade tumors.

The prognosis depends primarily on the grade of the tumor. Patients with low-grade tumors have a very good prognosis, with more than 95% of patients surviving 5 years. In contrast, only 40% of patients with high-grade tumors survive 5 years.

NAME: Acinic cell carcinoma

Etiology: The etiology of **acinic cell carcinoma** is unknown.

Epidemiology: The mean age for development of this tumor is 45 years, but it can be found any time between the ages of 20 and 70 years. Acinic cell carcinoma appears equally in women and in men.

Pathogenesis: Acinic cell carcinomas arise from serous cells within the major salivary glands. Mutations in chromosomal DNA are thought to initiate the neoplastic process. The parotid gland is affected most often, followed by the submandibular gland and then minor salivary glands.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: When found in the parotid or submandibular glands, these tumors present as slow-growing hard masses. In parotid tumors, facial nerve paralysis occurs infrequently but indicates a less than favorable prognosis. Minor salivary gland tumors appear as

FIGURE 17.28. Acinic cell carcinoma. This malignancy usually arises in the major salivary glands; however, here, it is pictured in the upper lip.

slow-growing masses on the palate, buccal mucosa, or lips more often than any other intraoral area (Fig. 17.28). Pain can be a symptom no matter where this tumor is located and is not related to the degree of tumor involvement; it does not indicate a less favorable prognosis.

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: Acinic cell carcinoma is characterized by a highly variable microscopic appearance.

Dental Implications: As noted above, these tumors are slow growing, and the dental hygienist may be the first person to detect this neoplasm during a periodic oral examination.

Differential Diagnosis: Clinically, acinic cell carcinoma may present as a painless mass similar to other salivary gland and soft tissue tumors. Biopsy is necessary to differentiate between these entities.

Treatment and Prognosis: Acinic cell carcinoma is a low-grade carcinoma with a relatively good chance of local recurrence, but only a slight chance of distant metastasis. Involvement of the parotid gland results in partial or total removal of the gland (often sacrificing the facial nerve in a total parotidectomy), depending on the location of the tumor. The entire submandibular gland is removed when tumors are found in this location. Minor salivary gland tumors are treated with surgical excision of the tumor including an adequate margin of normal surrounding tissue.

Prognosis is similar to that of mucoepidermoid carcinoma, which is generally good. About one-third of patients have a local recurrence, and distant metastasis develops in about 15%. The 5-year survival rate is about 90%. At 20 years, the survival rate is about 55%.

Minor Salivary Gland Malignancies

Polymorphous low-grade adenocarcinoma (PLGA) and adenoid cystic carcinoma are malignant tumors that primarily affect the minor salivary glands. Low-grade mucoepidermoid carcinoma, discussed above, is also frequently seen within the minor salivary glands.

NAME: Polymorphous low-grade adenocarcinoma (PLGA)

Etiology: The etiology of **polymorphous low-grade adenocarcinoma** (PLGA) and other salivary neoplasms may be associated with various genetic mutations and the overproduction of specific gene products including the protein p63.

Method of Transmission: Not applicable

Epidemiology: This lesion appears most frequently at about 60 years of age (range between 40 and 80 years of age).

Pathogenesis: Proliferation of salivary duct cells results in a slow-growing, submucosal mass.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: The palate is the most frequent site for PLGA. It presents as a slow-growing, smooth-surfaced, painless mass that may exist for years before discovery leads to diagnosis and treatment (Fig. 17.29). Large tumors may become ulcerated because of secondary trauma.

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: The ductal cells of this malignant neoplasm display different growth patterns, hence the name polymorphous.

Dental Implications: One of the first signs of a palatal growth might be a denture that starts to feel uncomfortable or loose. All patients who wear dentures should be encouraged to have periodic oral examinations to detect abnormalities in the early stages.

Differential Diagnosis: Biopsy is necessary to determine a definitive diagnosis for this soft tissue neoplasm. However, the following conditions should be included in a differential diagnosis:

1. Lymphoma, Chapter 9
2. Fibroma, Chapter 17
3. Neurofibroma, Chapter 17
4. Neurilemoma, Chapter 17
5. Adenoid cystic carcinoma, Chapter 17
6. Mucoepidermoid carcinoma, Chapter 17

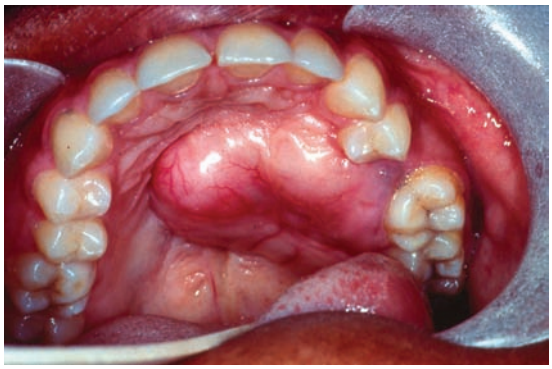

FIGURE 17.29. Polymorphous low-grade adenocarcinoma is found most often as a slow-growing mass in the hard palate as seen in this example. (Courtesy of Dr. George Blakey.)

Treatment and Prognosis: Surgical excision with wide margins is the treatment of choice for PLGA. Local recurrence has been reported but is usually managed by reexcision. Metastasis is considered an uncommon occurrence.

NAME: Adenoid cystic carcinoma

Etiology: The etiology of **adenoid cystic carcinoma** is unknown; however, some evidence supports an association with mutations on chromosomes 6 and 12 and deletion of genetic material from chromosome 19.

Method of Transmission: Not applicable

Epidemiology: This neoplasm is seen most frequently in the 40- to 60-year age group. Most studies have shown that gender distribution is equal.

Pathogenesis: Adenoid cystic carcinoma is a high-grade malignant tumor. This tumor arises most frequently within the minor salivary glands, followed by the parotid gland and the submandibular gland. The tumors are usually nonencapsulated and infiltrate the surrounding normal tissue.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: Parotid gland tumors present as firm, well-defined masses within the gland. They are slow-growing and may be tender on palpation. Facial nerve involvement may indicate that the tumor is in an advanced stage. Intraoral tumors occur on the palate more frequently than on any other surface, although these tumors can occur anywhere in the oral cavity (Fig. 17.30). The mucosal surface of adenoid cystic carcinoma is often ulcerated, especially when the lesion is found on the hard palate. Pain may be reported prior to any clinical evidence of the growth. In addition, palatal lesions may cause destruction of the underlying bone.

Distinguishing Characteristics: Intraoral lesions often manifest with pain as an early symptom.

FIGURE 17.30. Adenoid cystic carcinoma. Minor salivary glands are affected by this malignancy more often than the major salivary glands. The palate is the most common location for the development of adenoid cystic carcinoma, but it can occur on any intraoral surface as evidenced by this tumor found on the buccal mucosa.

Significant Microscopic Features: Adenoid cystic carcinoma is composed of cystic spaces and clusters of cells that form duct-like structures. The lesions have a tendency to invade the tissues surrounding nerve fibers (**perineural invasion**), which may account for the difficulty in managing adenoid cystic carcinoma.

Dental Implications: Radiation therapy is almost always recommended. Therefore, all dental procedures need to be accomplished prior to the radiation therapy. In addition, the patient needs to be instructed about the long-term management of xerostomia and other oral side effects of radiation.

Differential Diagnosis: Any soft tissue enlargement, especially those associated with surface ulceration, should be considered in a differential diagnosis of adenoid cystic carcinoma. The following are included:

1. Lymphoma, Chapter 9
2. Necrotizing sialometaplasia, Chapter 12
3. Traumatic fibroma, Chapter 17

Treatment and Prognosis: Surgical excision is the treatment of choice for adenoid cystic carcinoma. Removal of tumors within the parotid gland may require sacrifice of the facial nerve. Intraoral tumors should be removed with wide surgical margins. Removal of the underlying bone may be necessary with palatal lesions. Adjuvant radiation therapy is recommended for most tumors. Studies show that immunotherapy, in addition to surgery and radiation therapy, may prove useful in the future.

This tumor has a good 5-year prognosis and a poor 20-year prognosis.

Genetic and Congenital Disorders

Soft tissue enlargements in the oral cavity are often associated with genetic abnormalities or congenital malformations. Some of these are neoplastic, with the proliferative process being initiated by genetic abnormalities that cause the production of defective proteins or inhibit the action of tumor suppressor or DNA repair genes. Other enlargements are caused by abnormal development of tissues, such as lymphatic vessels, or the development of epithelium-lined cavities (cysts) that are derived from remnants of early epithelial tissues.

NAME: Neurofibromatosis, type 2B (von Recklinghausen disease of the skin)

Etiology: This is an inherited disorder that is associated with a mutation of the *NF1* gene (neurofibromatosis-1 gene) on chromosome 17. New genetic mutations that occur spontaneously, without any hereditary influence, may account for up to 50% of cases.

Method of Transmission: Neurofibromatosis is transmitted through an autosomal dominant inheritance pattern, or it occurs as a new mutation.

Epidemiology: It is estimated that 1 of every 3,000 individuals throughout the world is affected by this disorder. However, many feel that this estimate is low because of misdiagnosis or nonidentification of cases in which the manifestations are very mild. All races and ethnic groups are equally affected as are both genders.

Pathogenesis: Genetic abnormalities in the *NF1* gene cause decreased production of neurofibromin, a substance that functions as a tumor suppressor. The manifestations of this deficiency range from mild to severe and appear in organs and tissues throughout the body.

Extraoral Characteristics: The typical manifestations associated with neurofibromatosis include the following:

- Multiple neurofibromas, including small superficial cutaneous and subcutaneous lesions (Fig. 17.31), large cutaneous and subcutaneous lesions, and plexiform neurofibromas. Plexiform neurofibromas are large, diffuse growths that invade deeper tissues and can cause pain and destruction of bone.
- **Café au lait macules** (flat areas of hyperpigmented skin) are usually the first manifestation of this disorder, appearing in early childhood and increasing in number and size throughout life (Fig. 17.32). In addition, patients almost always present with axillary (under the arms) or inguinal (groin area) freckles that develop sometime during childhood.
- Lisch nodules (freckling within the iris of the eye) are also seen frequently in this condition (Fig. 17.33).
- Individuals usually have a short stature and other bone abnormalities, which include thinning of the cortical bone leading to bowing of the legs; sphenoid dysplasia, which can lead to herniation of the brain through the defective sphenoid bone; scoliosis (curvature of the spine); and destruction of the knee joints.

FIGURE 17.31. Neurofibromatosis. This female patient presented with multiple neurofibromas on the face and other cutaneous surfaces.

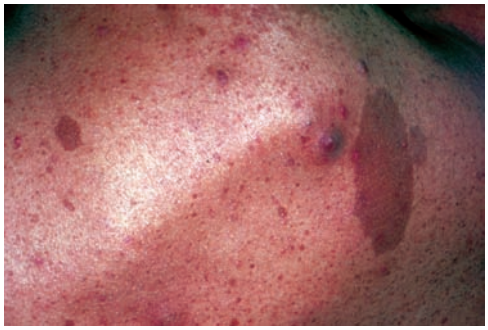

FIGURE 17.32. Multiple café au lait macules are seen on the upper back of an individual diagnosed with neurofibromatosis. (From Goodheart HP. Goodheart's photoguide of common skin disorders. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

- Seizures due to intracranial neurofibromas are present in 4 to 7% of cases.
- Many individuals have learning disabilities and may have poor eye–hand coordination.
- Hypertension is often associated with growths in the adrenal gland or a specific form of kidney disease that is common in these individuals.

Diagnosis of this condition usually depends on identifying the clinical manifestations and knowing the genetic background of the individual. Included in the diagnostic criteria are the following: (1) a first-degree relative with the condition, (2) six or more café au lait macules or freckling in the axillary or inguinal regions, (3) Lisch nodules, (4) optic glioma, (5) the presence of two or more neurofibromas or one plexiform neurofibroma, and (6) characteristic bone changes. An individual who meets any two or more of these criteria is highly suspected to have the condition. Individuals who have neurofibromatosis have a 10% lifetime risk for developing malignant peripheral nerve sheath tumors or a neurosarcoma within a preexisting neurofibroma.

Perioral and Intraoral Characteristics: Neurofibromas and café au lait macules can appear on the face and lips.

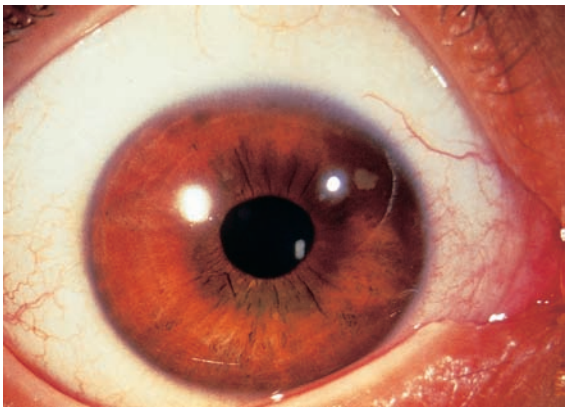

FIGURE 17.33. Lisch nodules. Freckling seen within the iris is consistent with a diagnosis of neurofibromatosis. (From Tasman W, Jaeger E. The Wills Eye Hospital atlas of clinical ophthalmology. 2nd ed. Baltimore: Lippincott Williams & Wilkins, 2001.)

Multiple intraoral neuromas are seen in approximately 25% of patients. These appear on any intraoral surface as well-defined, painless, submucosal nodules. Lesions of the tongue can appear as macroglossia.

Distinguishing Characteristics: The cutaneous manifestations, including multiple café au lait macules, Lisch nodules, and axillary or inguinal freckling, are characteristic of this disease.

Significant Microscopic Features: Features are identical to the microscopic features of the solitary neurofibroma.

Dental Implications: The appearance of neurofibromas in the oral and perioral area is common. Problems associated with the development of these lesions include impaired mastication, swallowing, and speaking. Lesions can become chronically traumatized if they are near the plane of occlusion. The growths may complicate the patient's attempts to maintain good oral hygiene. The hygienist may be asked to suggest home care modifications to alleviate this problem. Dental health care providers should evaluate the oral soft tissues and bone for any clinical or radiographic changes indicating malignant transformation of these tumors.

Differential Diagnosis: This disease is not easily confused with any other disorder.

Treatment and Prognosis: Neurofibromatosis is a genetic disorder and therefore cannot be treated in the strict sense of the word. Management of neurofibromatosis includes frequent examination of the skin for new lesions and assessment of already present lesions for the development of malignant changes. Surgical resection of lesions that are causing problems because of their location or for cosmetic reasons is beneficial. However, in many cases, there are so many lesions it is impossible to remove them all. The tendency for the lesions to recur makes surgical management even more difficult. Children should have an annual evaluation of the spine to identify and treat scoliosis in the early stages. All patients should have periodic assessment of their blood pressure to identify kidney problems. Patients with this genetic disorder should receive genetic counseling to help with future life choices (Pletcher, 2006).

Generally speaking, neurofibromatosis decreases life expectancy by about 15 years. This is due to the complications of hypertension and the increased chance of a malignancy occurring (Pletcher, 2006).

NAME: Multiple endocrine neoplasia syndrome, type 2B (MEN 2B, mucosal neuroma syndrome)

Etiology: MEN syndromes are genetic disorders caused by mutation of a protooncogene (*RET*) located on chromosome 10. These are inherited tumor syndromes and affect certain endocrine organs that originate from neural crest cells. MEN syndromes are classified as types 1, 2A, and 2B. MEN 2B is the more aggressive type MEN 2.

Method of Transmission: The genetic mutation can be inherited as an autosomal dominant trait or it can occur spontaneously as a new mutation.

Epidemiology: MEN 2B is rare and is distributed equally among racial and ethnic groups but is seen twice as often in males than in females.

Pathogenesis: Mutation and subsequent activation of the *RET* protooncogene causes hyperplasia of the target cells located in the thyroid and adrenal glands and in mucosal tissues, which leads to tumor formation in these tissues.

Extraoral Characteristics: The facial and oral characteristics of MEN 2B are the first features of the syndrome that are observed. Most of these individuals have a tall, slender body with long arms often referred to as a *marfanoid* body type because of the similarity to the body type seen in Marfan syndrome (see Chapter 6). Aggressive thyroid cancer (medullary thyroid carcinoma) can appear as early as 1 year of age, with 5% of cases occurring prior to the age of 5 years. Adrenal gland tumors (pheochromocytoma) also occur early in these patients, and constant medical follow-up is required to watch for neoplastic changes. Adrenal gland tumors cause flushing, heart palpitations, diffuse sweating, and diarrhea. Mucosal neuromas may occur on any mucosal surface. Intestinal neuroma or ganglioneuromatosis is a common finding in MEN. In addition, neuromas are often seen on the eyelids or cornea.

MEN 2A does not manifest with the marfanoid body type or the mucosal neuromas seen in 2B. A less aggressive thyroid cancer is also seen in type 2A. MEN type 1 is not commonly associated with thyroid cancer and normally presents with tumors of the parathyroid glands and pancreatic islet cells. Pituitary hyperplasia or tumors are also seen in this type of MEN (Lendel et al., 2010).

Perioral and Intraoral Characteristics: Patients commonly exhibit a wide-eyed expression and mandibular prognathism, as well as malocclusion and diastemata between the maxillary central incisors. Mucosal neuromas can be found on the lips, tongue, and any other oral mucosal surface. The lips may appear puffy and protuberant because of multiple neuromas. The palate may be high-arched and narrow, a finding that is not related to the presence of neuromas but to the general marfanoid body type that is manifest. The tongue is a common location for formation of multiple neuromas, and macroglossia due to these tumors is often seen (Fig. 17.34). These are usually the first signs of MEN 2B.

Distinguishing Characteristics: Mucosal neuromas, pheochromocytomas, and medullary carcinoma of the thyroid are the distinctive elements of this syndrome.

Significant Microscopic Features: The mucosal neuromas display marked hyperplasia of nerve bundles in a loose connective tissue background.

Dental Implications: The dental hygienist may be the first health care provider to detect mucosal neuromas in a young child during a routine oral examination. Neuromas are an early sign of the disorder and Usami et al. (2011)

FIGURE 17.34. Multiple endocrine neoplasia syndrome, type 2B. Multiple mucosal neuromas indicate this disorder. Pictured here are several mucosal neuromas on the tongue.

stresses the importance of early recognition and detection of the disease in order to make an appropriate medical referral. Prompt diagnosis of this condition is crucial in preventing thyroid cancer and ensuring the individual has every chance of a long life.

Differential Diagnosis: The mucosal neuromas associated with MEN 2B resemble the neurofibroma, fibroma, and lipoma (all in Chapter 17). If macroglossia is present, congenital malformations such as lymphangioma and hemangioma and metabolic conditions such as amyloidosis should be considered in the differential diagnosis.

Treatment and Prognosis: Treatment of the syndrome includes prophylactic removal of the thyroid, often during infancy but almost always prior to the age of 5 years for those with an identified *RET* mutation (Richards et al., 2012). Removal of the thyroid is followed by continual monitoring of blood calcitonin levels. Increased levels of calcitonin indicate a recurrence of the thyroid tumor. Adrenal gland tumors are benign but have the ability to cause significant hypertension and other cardiovascular problems. Surgical removal of these tumors is also recommended. Mucosal neuromas are usually surgically excised and are not expected to recur.

The prognosis is good if the disease is identified early and the thyroid prophylactically removed. If medullary carcinoma of the thyroid does occur, the prognosis is poor, with a 5-year survival rate of only 50%.

NAME: Lymphangioma

Etiology: The etiology of **lymphangiomas** is unknown. Some may be associated with an inherited trait that has yet to be identified.

Method of Transmission: Lymphangioma may have a genetic tendency relative to its congenital presentation, but otherwise, it is not transmissible.

Epidemiology: Lymphangiomas are relatively rare in the United States, accounting for about 4% of all vascular tumors (Schwartz & Fernandez, 2012). Lymphangioma affects whites more often than other races but affects males and females equally. It is usually evident at birth or in early childhood.

FIGURE 17.35. A large cystic hygroma in the neck of an infant. (Courtesy of Dr. John Jacoway.)

Pathogenesis: Lymphangioma is a congenital malformation of lymphatic vessels thought to be associated with islands of misplaced embryologic lymph tissue that develop independently of the lymph system and grow as the child grows. These growths are considered hamartomas. The lesions do not regress as the child ages. Lymphangiomas may be superficial or located deep within tissues.

Extraoral Characteristics: The most common location of lymphangioma is the head and neck area. One specific form of lymphangioma, **cystic hygroma,** affects the neck and submandibular spaces (Fig. 17.35). Cystic hygromas may cause respiratory obstruction and become life threatening. Rapid enlargement of a cystic hygroma can occur when there is trauma to the area or when there is a respiratory or oral infection that results in an inflammatory response.

Perioral and Intraoral Characteristics: Superficial lymphangiomas present as painless nodules that may be translucent or bluish and have a pebbly or bubbly surface that looks somewhat like cooked tapioca. Blood vessels that may develop within the lesion can impart a darker red to blue color (Fig. 17.36). Deeper lesions present as submucosal swellings that are poorly defined and distort the local anatomy. When these lesions are palpated, movement of the lymph fluid within them may produce a crackling sound (**crepitus**). The tongue and buccal mucosa are the most common sites for lymphangiomas in the oral cavity. Large tongue lesions can cause macroglossia.

Distinguishing Characteristics: The pebbly surface texture of superficial lesions and evidence of crepitus on palpation are significant features that can help to identify this lesion.

FIGURE 17.36. Lymphangioma. Note the bluish color caused by the growth of blood vessels within the lesion and the pebbly surface of this superficial lymphangioma of the tongue. (Courtesy of Dr. Robert J. Gorlin.)

Significant Microscopic Features: The lesion is composed of endothelial-lined, thin-walled channels that are found just beneath the epithelial surface.

Dental Implications: Patients who have had surgical removal of a lymphangioma may have damage to the facial, lingual, or hypoglossal nerves. The dental hygienist is in an excellent position to help the patient learn how to manage the complications associated with some of this damage.

Differential Diagnosis: Most of the other soft tissue enlargements that present in the oral cavity may need to be differentiated from this lesion. Some of those include the following:

1. Hemangioma, Chapter 13
2. Mucocele and ranula, Chapter 11
3. Dermoid cyst, Chapter 17
4. Branchial cleft cyst, Chapter 17
5. Cellulitis, Chapter 3
6. Thyroglossal duct cyst, Chapter 17

Treatment and Prognosis: Treatment depends on the size, location, and composition of the malformation. Small lesions may not need to be treated at all unless they create a cosmetic problem. Surgical removal of lymphangiomas is the treatment of choice for other lesions, even though there is a 20 to 40% postsurgery recurrence rate. Large lesions in the tongue can be difficult to manage because it is not desirable to remove large portions of the tongue. In cases like this, other therapies, such as laser and sclerotherapy, can be used in conjunction with surgery to produce a better result. Laser therapy is used to control the size of growing lesions and as an adjunct to surgical removal in most cases. Some small superficial lesions may be eradicated with laser therapy alone. Sclerotherapy uses chemical agents injected directly into the lesion to cause an inflammatory reaction that results in scar tissue formation and subsequent destruction of the lesion or reduction in size.

The prognosis for small, isolated lesions is excellent. The prognoses for larger lesions and the cystic hygroma are based on the location and size of the lesion and its involvement with adjacent vital structures. Complications from surgery occur frequently and include airway obstruction, infections, hematomas, and nerve damage. Mortality rates from the lesions or from complications of surgery range from 2 to 12%.

Soft Tissue Developmental Cysts

The formation of these developmental **cysts** (epithelial-lined, fluid-filled cavities) is associated with remnants of epithelial tissues left after embryologic development of the structures is completed. These lesions all present as smooth-surfaced masses that are somewhat rubbery to palpation. They are only visualized easily when they have grown to a fairly large size. However, they can be detected much earlier in the course of their development by thorough head and neck examinations performed by the dental hygienist or dentist. Failure to include palpation as an examination method will often lead to missing these lesions.

NAME: Cervical lymphoepithelial cyst (branchial cleft cyst)

Etiology: Historically, this lesion was thought to develop from remnants of the second branchial arch. A more recent theory suggests that it arises from parotid gland epithelium that becomes entrapped within cervical lymph nodes.

Method of Transmission: Not applicable

Epidemiology: These lesions are usually detected in young adults between the ages of 10 and 40 years, and there is no gender predilection.

Pathogenesis: Parotid gland epithelium that is trapped within a cervical lymph node begins to proliferate and eventually forms a cyst. The cyst enlarges as the epithelial cells continue to proliferate.

Extraoral Characteristics: The cervical lymphoepithelial cyst is normally located along the anterior border of the sternocleidomastoid muscle. It is soft and **fluctuant** (manifests a wave-like feeling) when palpated. It is seen more often on the left side but can be found anywhere in the general vicinity of the sternocleidomastoid muscle (Fig. 17.37). Occasionally, lesions will become infected, and formation of an abscess within the cyst is possible. In most cases, the cysts are asymptomatic, but drainage to the exterior surface of the skin may develop.

Perioral and Intraoral Characteristics: The intraoral counterpart is called a lymphoepithelial cyst and is commonly found in the floor of the mouth and the posterior lateral border of the tongue.

Distinguishing Characteristics: The intraoral lesions often have a pale yellowish hue.

FIGURE 17.37. Cervical lymphoepithelial cyst. This lesion presents as a right neck mass in the area of the anterior border of the sternocleidomastoid muscle.

Significant Microscopic Features: The epithelium lining the cyst is composed of stratified squamous and/or pseudostratified columnar epithelium supported by connective tissue containing lymphoid cells.

Dental Implications: It is essential for the dental health care provider to consistently provide examinations that include palpation of the neck and soft tissues of the face to detect abnormalities at an early stage.

Differential Diagnosis: Any soft tissue enlargement that could occur in this area should be considered in a differential diagnosis. Some of the more likely lesions include the following:

1. Lymphadenopathy, which occurs as a symptom or sign of many disorders and diseases and is found in conditions discussed throughout this text
2. Vascular neoplasm or malformation, Chapter 13
3. Lipoma, Chapter 17
4. Cystic hygroma, Chapter 17

Treatment and Prognosis: Complete surgical excision is recommended. The prognosis is good; however, untreated growths are prone to recurrent infections and abscess formation.

NAME: Thyroglossal tract cyst

Etiology: The **thyroglossal tract cyst** results from a proliferation of remnants of epithelial cells that lined the thyroglossal tract during embryonic development.

Method of Transmission: None

Epidemiology: The cyst is considered the most common of the developmental cysts of the neck, making up 2 to 4% of all neck masses. Thyroglossal tract cysts are seen more often in children. The lesion is seen equally among males and females and among ethnic groups.

Pathogenesis: This cyst originates in the embryologic development of the thyroid gland, which occurs within the posterior portion of the tongue at the foramen caecum. The immature thyroid tissue migrates down an epithelial duct or tract to its permanent location at the level of the thyroid cartilage at about the 7th week of embryonic development. Although the thyroglossal duct epithelium normally undergoes atrophy, occasionally remnants remain and proliferate, forming the thyroglossal tract cyst.

Extraoral Characteristics: Most of these cysts are found in the midline of the neck where they appear as well-circumscribed, nontender, mobile masses, usually between 2 and 4 cm in diameter (Fig. 17.38). Often, dysphagia and **dysphonia** (a change in voice quality) accompany larger lesions. In addition, airway restriction is noted occasionally. Moorthy and Arcot (2011) found that in a study of twenty-four patients, most exhibited symptoms and two patients were diagnosed with a malignancy. The symptoms exhibited included: pain, dyspnea, dysphagia, and discharge. The two patients found to have malignancy were asymptomatic. This fact is reported because even in malignancy, the symptoms reported by patients will vary and the growth is sometimes not painful. The lesions have a tendency to become infected, and draining fistula tracts may develop.

Perioral and Intraoral Characteristics: About 2% of these lesions develop within the tongue itself (lingual thyroid). Rarely, these will appear in the suprahyoid position as a swelling of the floor of the mouth.

Distinguishing Characteristics: Not applicable

FIGURE 17.38. The fluctuant mass seen in midline of the neck is a thyroglossal tract cyst.

Significant Microscopic Features: The lesion displays a central cavity lined with stratified squamous, columnar, and/or cuboidal cells. Some thyroglossal tract cysts contain actual thyroid tissues peripheral to the epithelial lining.

Dental Implications: Lesions located on the posterior dorsal surface of the tongue should not be removed until it is known what they are, because there is a chance that a mass in this location may contain the patient's only thyroid tissue.

Differential Diagnosis: As noted above, biopsy is the only way to definitively diagnose any of these lesions. A few lesions that would be included in a differential diagnosis of this condition include the following:

1. Dermoid cyst, Chapter 17
2. Thyroid neoplasms, which are clinically similar to the thyroglossal tract cyst; biopsy is the only way to determine a definitive diagnosis of this type of lesion.
3. Branchial cleft cyst, Chapter 17
4. Epidermoid cyst, which has clinical features identical to the dermoid cyst but does not have dermal appendages within the cyst wall.
5. Goiter, Chapter 7

Treatment and Prognosis: Complete surgical excision using the Sistrunk procedure (includes removal of the midsection of the hyoid bone) is the treatment of choice after testing to determine the presence of other functioning thyroid tissues in the normal location. If complete excision is not accomplished, there is a 3 to 5% chance of recurrence. Recurrence is also associated with a history of repeated infections. Prognosis is normally excellent if the cyst is completely excised. There is a very slight risk of malignant transformation of this lesion, especially if it has recurred after excision and has a history of repeated infection.

NAME: Dermoid cyst

Etiology: Dermoid cysts result from the entrapment of epithelial cells along the lines of embryonic closure or fusion. They are, therefore, located in the midline in the head and neck region and are sometimes evident in the floor of the mouth.

Method of Transmission: Not applicable

Epidemiology: This is an uncommon oral cyst that usually appears between the ages of 10 and 30 years. It is seen equally in males and females and across all ethnic groups.

Pathogenesis: These cysts develop from bits of epithelium trapped in embryonic lines of fusion. Proliferation of this epithelium leads to the development of an epithelial-lined cavity containing sebaceous glands, sweat glands, hair follicles, and sometimes tooth-like structures.

FIGURE 17.39. Dermoid cyst. When this cyst occurs intraorally, it is seen in the floor of the mouth.

Extraoral Characteristics: The related teratoid cysts (neoplasm composed of multiple tissues not normally found in the organ in which it arises) are uncommon tumors that can develop in any area of the body. If this cyst contains elements from all three embryonic germ layers, it is called a **teratoid cyst**.

Perioral and Intraoral Characteristics: The dermoid cyst develops as a painless, slow-growing, soft, doughy, midline mass, primarily in the floor of the mouth (Fig. 17.39). It can be located superior to the mylohyoid muscle and cause the tongue to be displaced superiorly and posteriorly, or it can be located inferior to the muscle and appear as a swelling in the midline of the neck.

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: The dermoid cyst displays a central cavity lined by orthokeratotic stratified squamous epithelium supported by a connective tissue wall containing sebaceous glands, sweat glands, and hair follicles. Large amounts of keratin and sebum from the glands in the connective tissue wall fill the cavity.

Dental Implications: If this lesion is located in the floor of the mouth, it can impair chewing, swallowing, and speaking. Patients may present with this as a reason for seeking dental care.

Differential Diagnosis: Some of the disorders identified in a differential diagnosis of this type of lesion include the following:

1. Thyroglossal tract cyst, Chapter 17
2. Salivary gland enlargements (including ranula), Chapter 17
3. Salivary gland neoplasms, Chapter 17
4. Cystic hygroma, Chapter 17

Treatment and Prognosis: Treatment is surgical excision. The prognosis is excellent. There is a slight chance of malignant transformation in dermoid cysts that have been present for a long time.

SUMMARY

- Soft tissue enlargements are associated with reactive (traumatic), genetic, neoplastic, or developmental processes. The lesions arise from epithelial, endothelial, or connective tissues, and they can be benign or malignant.
- Lesions that are associated with trauma or inflammation can be linked to a specific cause that initiates the adaptive hyperplastic cellular response.
- Traumatic neuromas occur in areas where a nerve has been traumatized. Pain on palpation is often associated with this lesion.
- Fibromas are the most common soft tissue tumor found in the oral cavity. They occur most often in areas that are traumatized frequently. Denture-induced fibrous hyperplasia is a variant of the same process.
- Cowden syndrome is characterized by multiple facial and oral fibrous papules. Individuals with this disorder have a higher than normal risk of developing thyroid and breast cancers.
- The peripheral ossifying fibroma (three histologic forms) is a reactive lesion found exclusively on the attached gingiva.
- Drug-induced generalized gingival hyperplasia is associated with phenytoin, calcium channel blockers, and some immunosuppressants (cyclosporine). Hormone-related gingival hyperplasia usually occurs when hormone imbalances or spikes occur in different stages of life, such as pregnancy and puberty. The presence of dental biofilm enhances the hyperplastic process.
- Lymphoid hyperplasia is a reactive response that is part of the normal immune system function. Waldeyer ring and the posterior lateral and dorsal portions of the tongue are common places to find lymphoid hyperplasia.
- Sarcoidosis is a multisystem inflammatory disease that may manifest with salivary gland enlargement, nodular growths on the oral mucosal surfaces, and xerostomia.
- Mumps is a viral infection of the glandular tissues, most often affecting the parotid gland.
- Individuals with xerostomia have the highest risk of developing bacterial sialadenitis, which is characterized by painful swelling of the gland and a purulent exudate from the gland orifice.
- Sjögren syndrome occurs in a primary form as isolated destruction of exocrine glands (salivary and lacrimal specifically) or as a secondary form combined with another autoimmune disorder such as rheumatoid arthritis.
- Fibromatosis is an aggressive benign tumor that has no potential for metastasis.
- Most oral soft tissue neoplasms present as slow-growing, painless masses that cannot be differentiated from each other on the basis of clinical appearance or behavior alone. A biopsy is necessary to obtain a definitive diagnosis.
- The neurilemoma, neurofibroma, neuroma, fibroma, and lymphangioma frequently appear as submucosal swellings on the tongue.
- The leiomyoma (benign) and leiomyosarcoma (malignant) are neoplasms of smooth muscle tissue. The rhabdomyoma (benign) and rhabdomyosarcoma (malignant) are neoplasms of striated muscle. The rhabdomyosarcoma is the most common soft tissue sarcoma seen in children.
- The pleomorphic adenoma is the most common form of benign salivary gland neoplasm. It affects the major salivary glands more often but may also be found in the minor glands.
- Frey syndrome is often seen in individuals who have had parotid gland surgery. It is characterized by facial sweating on the affected side when nervous stimulation of the salivary glands occurs.
- Papillary cystadenoma lymphomatosum is a relatively common salivary gland tumor that develops most often in the tail of the parotid and is associated with smoking tobacco.
- Mucoepidermoid carcinoma is the most common salivary gland malignancy in the United States, affecting both major and minor salivary glands.
- Neurofibromatosis is a common genetic disorder that manifests with very distinctive cutaneous and oral conditions. Café au lait macules (six or more), Lisch nodules, and multiple neurofibromas are elements of the diagnostic criteria.
- Multiple endocrine neoplasia syndromes, specifically MEN 2B, present with multiple mucosal neuromas and other general physical findings. Early identification of individuals with this disorder is crucial to prevent the development of a very aggressive thyroid cancer.
- Lymphangiomas are hamartomatous tumors that may present intraorally with a pebbled surface and crepitus on palpation. Cystic hygromas are a form of lymphangioma that affects the large spaces of the neck and can produce respiratory distress.
- The cervical lymphoepithelial cyst, dermoid cyst, and thyroglossal tract cyst are all developmental cysts associated with the proliferation of entrapped embryonic epithelial tissues. They are most commonly observed in the neck region or the floor of the mouth.

CHAPTER REVIEW

Case Study 17.1

Carlos, a 25-year-old man, comes to your school's dental hygiene clinic for an initial appointment. His health history is unremarkable except for the fact that he quit smoking 4 years ago. He is taking no medication at this time but does report an allergy to aspirin. His vital signs are within normal limits. There are no positive findings from the extraoral examination. However, during the intraoral examination, you discover the tongue lesion depicted in Figure 17.40.

1. Write a clinical description of this lesion from what you can observe.
2. Develop a preliminary differential diagnosis for this lesion from what you observe in the figure.
3. What would you like to ask the patient about this lesion?

As you continue your examination, you palpate the tongue and feel a wave-like movement or vibration with very slight crackling (crepitus) as you palpate the lesion. The lesion blanches slightly when palpated. The patient reports no pain and tells you that the lesion has been there as long as he can remember. He also states that it was much smaller when he was young, but that it got larger when he was a teenager. It hasn't gotten any larger for quite a few years, though.

4. What important information has he just relayed to you and what could it mean?
5. Determine the most likely diagnosis from your differential diagnosis.
6. Is there any way that you can obtain a definitive diagnosis for this lesion without performing a biopsy?

FIGURE 17.40. Courtesy of Dr. Peter Jacobsen.

For answers and additional review activities, log in to **thePoint.lww.com**

Case Study 17.2

The patient depicted in Figure 17.41 is a 16-year-old female named Laura who noticed the lesion on the ventral tongue over a year ago. She believes that the red area has become larger in the last few months and has come into your practice today because she believes that she has cancer. She is a nonsmoker and does not use alcohol but has read that the tongue is a high-risk area for malignancy. She tells you that she has learned that certain cancers have been rising in her age group, even for people who do not engage in behaviors such as drinking and smoking. What would you tell her and what is your best differential diagnosis with regard to this lesion?

For answers and additional review activities, log in to **thePoint.lww.com**

FIGURE 17.41. Courtesy of Dr. Janete D. Almeida.

Critical Thinking Activity

What characteristics would you need to observe in a lesion or what information would you have to have about a lesion before you would recommend that it be biopsied? Why?

Portfolio Possibilities

- Prepare an office manual segment that illustrates correct palpation techniques for detecting masses of the neck and intraoral masses that could be cysts or neoplasms.
- Prepare an office manual segment listing the contact numbers for those practitioners who may need to be contacted for management of the patient who presents with a mass that could be a benign or malignant mesenchymal tumor. These contact numbers would include, but not be limited to, numbers for a(n):
  - Oral and maxillofacial surgeon
  - Oral and maxillofacial pathologist
  - Oncologist
  - Otolaryngologist
  - Hospital or imaging facility that could provide magnetic resonance imaging (MRI) or computerized tomography (CT)

Media Menu

American Cancer Society
http://www.cancer.org/

National Organization for Rare Diseases
http://www.rarediseases.org/

Sjogren's Syndrome Foundation
http://www.sjogrens.org/

World Health Organization
http://www.who.int/en/

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Take advantage of additional online resources to help you study and ace your exams!

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- Supplemental References

Online resources and links are available at http://thepoint.lww.com/DeLong2e.

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Chapter 17 **LESION/CONDITION SUMMARY TABLE**

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Traumatic neuroma	Chronic or acute trauma that severs a nerve. May occur due to the administration of anesthesia.	Trauma to the nerve is followed by ineffective and unregulated nerve regeneration.	Appear as small nodules that are firm and covered by normal mucosa. Usually painful when palpated. The tongue and lower lip are prime areas because of frequent trauma.	Irregular nerve bundles with dense fibrous connective tissue. Inflammatory cells are not usually seen.	Surgical removal is performed. There is a low rate of recurrence.	The pain may persist even after removal. Monitoring is needed.
Fibroma (focal fibrous hyperplasia, irritation fibroma, traumatic fibroma)	Fibromas are not true neoplasms, but reactive responses to chronic trauma.	The fibromas can be found on the tongue and palate and under dentures (denture-induced fibrous hyperplasia).	Exuberant growth of tissue is noted and commonly found in areas of high friction or trauma. The tissue may be the same color as surrounding tissue or in some cases more irritated or ulcerated.	Nodular excess of collagen fibers with sparse amounts of inflammatory cells	Surgical removal of the growth and the source of the trauma should be corrected. A new and better-fitting denture should be constructed.	If the source of the trauma is not removed, the growth may recur.
Cowden syndrome (multiple hamartoma syndrome)	Autosomal dominant syndrome	Rare disorder in which patients develop thyroid cancer, colon cancer, and breast cancer. Men may also have a higher risk of breast cancer.	Patients develop facial papules, small 1–5 mm that are flat topped, flesh-colored growths. Oral papules are 1–3 mm, smooth-surfaced, and the same color as surrounding tissue.	Collagen overproduction. Fibroblasts are visible.	Surgical removal	The dental professional may be the first person to note the oral manifestations and make a diagnosis of Cowden syndrome. When multiple fibromas are present in the adult, the clinician may make a referral for further investigation.
Peripheral ossifying fibroma	A reactive hyperplastic lesion that appears exclusively on the gingiva	Local factors such as calculus or some other type of foreign body initiate the hyperplastic process	A well-defined, firm, pedunculated or sessile, exophytic mass on the attached gingiva, usually interproximal, <1 cm in size.	Surface ulceration in most cases; POF contains bone and deposits of cementum. Giant cell fibromas contain multinucleated giant cells. Peripheral odontogenic fibroma is distinguished with odontogenic epithelium within the connective tissue. The three cannot be distinguished on clinical appearance—biopsy is needed.	Surgical removal	If the initiating factors are removed, the prognosis is good.
Generalized gingival hyperplasia	A generalized overgrowth of hyperplasic tissue. Most commonly, an exuberant response to chronic inflammation such as calculus, inadequate oral hygiene, medication, biofilms, and hormonal fluctuations.	Unknown, but it is thought to be the result of individual susceptibility. The presence of excessive amounts of keratinocyte growth factor.	Hyperplasia may be inflammatory or fibrotic and may be generalized or limited to a specific area. The hyperplasia can be mild to severe.	Excess amounts of fibrous connective tissue with or without inflammation	Discontinuance of offending products, increased efforts toward dental hygiene, and surgical removal of the hyperplasia may be needed in some cases. Drug-induced hyperplasia may resolve after discontinuing the medications.	The medical and dental history is important in determining the etiology. The hyperplasia may recur if the patient continues the medication. In other cases, after a stimulus is removed, the hyperplasia may resolve and not reappear.
Lymphoid hyperplasia	Proliferation of lymph cells within lymph tissues	Lymphoid tissue is involved in both the identification and processing of viruses, bacteria, and other invaders of the host. Lymphoid hyperplasia increases the chance that the host will be able to destroy the invaders.	Lymphoid tissue is abundant in the mouth and is dense in Waldeyer ring. Enlargements may be bullous, papillary, or smooth. Hyperplasia may involve the tonsillar tissue or the lateral border of the tongue. Foliate papilla may be enlarged as well.	Proliferation of lymphocytes and the presence of numerous macrophages	Identification is important to rule out cancer. Referral to an ear, nose, and throat specialist may be needed.	A diagnosis should be established and follow-up with the patient is necessary. Good recall maintenance and monitoring are needed.

continues

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Sarcoidosis	A multisystem inflammatory disease. The etiology is unknown. Mycobacteria and Epstein-Barr virus have been suggested in some cases. Current research indicates that both genetic and environmental factors and occupational causes play a role in the development.	Granulomas form in affected organs and tissues. Sarcoidosis is recognized as an exuberant immune response to an unknown antigen. Lymphocytes and macrophages, mast cell and natural killer cells, perpetuate the immune response and cause a chronic inflammatory process that results in the formation of granulomas.	Salivary gland enlargement is noted, especially in the parotid gland. Xerostomia usually occurs and oral lesions present as growths on the lips, gingiva, palate, and buccal mucosa.	Granulomas surrounded by an intense infiltrate of lymphocytes and multinucleated foreign body giant cells are characteristic.	Surgical removal is needed.	Patients will vary in their symptoms and sometimes these may include oral problems. Other disease states may have similar characteristics such as salivary gland enlargements, mucosal nodules, etc. A differential diagnosis may include eating disorders, diabetes, alcoholism, and other disease states exhibiting xerostomia. Referring to a physician and working closely with the patient's physician is crucial.
Ranula	A descriptive term used to describe a swelling in the floor of the mouth	Obstruction/injury to the submandibular and sublingual salivary gland resulting in an inflammatory response	Clinical manifestation of a mucocele. If the lesion herniates through the mylohyoid muscle, it is called "a plunging ranula" and appears in the area of the neck.	Mucous, salivary duct tissue	Surgical removal with marsupialization is usually needed.	Patients may be concerned with large swellings in the floor of the mouth. Other disease states may be cysts, mucoceles, and tumors. Reassurance is needed and explaining what has occurred to them is necessary.
Mumps	Paramyxovirus is transmitted by direct contact with saliva.	The most common presentation is the effect on the parotid gland and the swelling that ensues. The testes, pancreas, eyes, joints, kidneys, ovaries, and central nervous system may be involved.	The presence of swelling and systemic effects suggests the disease. The patient may experience pain while swallowing and chewing.	The virus may be detected by swabbing the buccal mucosa and nasopharynx areas. The virus can be found for up to 7 days before the initial symptoms and for 9 days following diminished symptoms.	Early detection is crucial since others may be exposed to the virus. Typical treatment for making the patient more comfortable is fine such as cold food, soft diet, fever reducers and a comfortable environment.	The focus is on relieving the general symptoms associated with a viral infection. The patient may experience pain while swallowing and chewing. Any treatment should be postponed until there is reassurance that the patient is no longer infectious.
Bacterial sialadenitis	Various pathogens such as *Staphylococcus aureus, Streptococcus viridans, Streptococcus pneumoniae,* and *Haemophilus influenzae*	Caused by an overgrowth of bacteria in a gland that is not producing adequate amounts of saliva. This produces both acinar and ductal inflammation.	Painful swelling of the affected gland. Trismus may occur. Purulent exudate may be present at the duct orifice.	Inflammation of the salivary gland. Culture of the exudate is important to determine the specific bacteria so that treatment is directed to the appropriate organism.	Identification of the specific bacteria, so that correct antibiotic can be administered. Analgesics, cold compresses and stimulation of the salivary glands.	Strategies to alleviate the xerostomia are crucial for the patient. Antibiotic therapy to eliminate the bacteria is performed.
Sjögren syndrome	Sjögren syndrome is a disorder that is usually found in women. Activated T cells infiltrate the salivary and lacrimal glands.	The acinar cells and gland ducts are attacked. Two forms exist: primary and secondary.	Most commonly associated with rheumatoid arthritis. Over 4,000,000 Americans are affected.	An increase of inflammatory lymphocytes that destroy salivary gland tissues	Xerostomia, dental caries, periodontal disease, and infections such as candidiasis require treatment with common protocol for each problem.	The symptoms of the disease are managed. Patients should be monitored since there is an increase in malignant transformation of the altered glandular tissue to lymphoma.
Fibromatosis (desmoid tumor)	May be associated with mutation of the cell's DNA or disruption of another defense against uncontrolled growth of cells	These lesions are aggressive but have no ability to metastasize.	When observed in the oral cavity, the fibromatosis is a slowly enlarging soft tissue mass. Asymmetry is noted as the lesions enlarge.	When in the bone, there is expansion of the cortical bone. The entity is seen as ill-defined radiolucencies.	Early recognition is important. Differentiation with the fibrosarcoma is crucial. Biopsy will confirm and differentiate fibromatosis from fibrosarcoma. Biopsy to confirm diagnosis is needed with surgical removal. Aggressive treatment is necessary with chemotherapy. The recurrence rate is 25%.	Follow up and monitoring of the patient is needed since there is the potential for recurrence.

Chapter 17 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Fibrosarcoma	A malignant tumor of fibroblasts. The etiology is obscure. May be linked with radiation exposure and tissue trauma.	The fibrosarcoma may be low or high grade.	Clinically, there may be pain, swelling, paresthesia, and loosening of the teeth with ulceration of the overlying mucosa.	Proliferating spindle cells are arranged in a herringbone pattern and mitotic figures are commonly observed.	Surgical excision with wide margins. There is local recurrence in 50 to 75% of cases. Distant metastasis occurs in 20–40% and the 5-year survival rate is 50–70%.	Early identification is crucial.
Neurilemoma (schwannoma)	Arises from the proliferation of the Schwann cells of the nerve sheath	Slow-growing tumor that can occur in soft tissues or bone. As Schwann cells proliferate, a fibrous capsule surrounds them. The nerve is pushed aside as the tumor grows.	Appear as small, smooth-surfaced, firm, nodular growths in the head and neck region. Or, in the flexor surfaces of the arms and legs. Usually painless unless they are very large and impinge on vital tissues. These occur most frequently on the tongue.	Microscopically, they appear as a mass of spindle-shaped cells surrounded by as fibrous capsule composed of residual nerve fibers and the connective tissue that forms the support structure for the peripheral nerves.	Accurate interpretation of radiographic findings in areas where a patient reports pain and paresthesia is essential and crucial.	Surgical excision and there is little chance of recurrence.
Neurofibroma	Benign neoplasm that originates from Schwann cells and/or connective tissue cells that support the peripheral nerves	Neurofibromatosis (von Recklinghausen disease of the skin) is an inherited syndrome characterized by multiple neurofibromas and other abnormalities.	The patient is usually in the fourth decade. Manifest as small, soft, nodular, sessile, or pedunculated growths. Most commonly found on intraoral structures of the tongue and the buccal mucosa.	When neurofibromas are in the bone of the maxilla or mandible, there is extensive expansion and destruction of bone. They are composed of spindle cells in a delicate connective tissue matrix. Mass cells are usually present.	The presence of multiple neurofibromas may indicate a relatively common genetic disorder called neurofibromatosis. The dental practitioner is in a unique position to seek medical evaluation for the patient.	Surgical excision. Excellent prognosis.
Leiomyoma	Benign neoplasm of smooth muscle	Commonly found in the muscular layer of the gut and in the uterus	Oral leiomyomas present as slow-growing, painless, smooth-surfaced masses usually <2 cm. Commonly found on the tongue, hard palate and buccal mucosa.	The malignant counterpart of this entity is the leiomyosarcoma that is a malignant neoplasm of the smooth muscle. The prognosis is poor with the malignant form. Early recognition is crucial.	Early diagnosis and removal are optimal. Differentiation of malignancy is needed through biopsy. More aggressive surgical procedures are needed with the malignant-type lesion of the leiomyosarcoma.	Surgical removal. Low chance of recurrence with the leiomyoma.
Rhabdomyosarcoma	Malignant tumor of striated muscle. The etiology is unknown.	Usually seen in children under 18 years old. A gene mutation is noted as well as a higher rate in certain birth defects.	The tumor is aggressive and spreads quickly. The orbital area is a prime location. Intraorally, the hard and soft palate is a prime location. Pain and paresthesia are common.	Biopsy is needed. Depending upon the location, a CT scan, bone scan, and MRI. Histology will vary depending upon the form of the neoplasm.	Early diagnosis and referral to a treatment center that specializes in this type of malignancy are optimal.	Complication may occur from chemotherapy, radiation, and surgery. Long-term survival is possible. Metastasis is also an issue of concern.
Lipoma	A benign neoplasm of adipose tissue. May occur in any area of the body. It is a common benign neoplasm. Usually found in adults 50+ years old.	Blunt force or soft tissue trauma is reported to occur prior to the development.	Appears as a superficial, smooth-surfaced, soft, palpable mass that often imparts a yellowish color due to the adipose tissue.	Lipoma may be slightly lighter in color with a yellow hue. This is in contrast to the fibroma that consists of fibrotic tissue. A thin, fibrous capsule surrounds the lipoma. Very little inflammation is present and removal is good because of the capsule.	The hygienist can be instrumental in detecting these types of lesions and also ruling out a potential malignancy. The counter part of the lipoma that is malignant is the fibrosarcoma.	Surgical removal is needed for true diagnoses through biopsy to rule out potential malignancy and also to confirm the lipoma diagnoses.
Pleomorphic adenoma	The tumor arises from the proliferation of glandular epithelium and myoepithelial cells. Some pathologists describe this entity and also use the term “mixed tumor.”	Alterations in chromosome 8 may be associated with the development of this tumor.	The tumor presents as a firm mass that is slightly compressible. It appears firm when in the plate region. It is slow-growing and painless.	The term “pleomorphic” is used to describe the highly variable microscopic appearance of the tumor. This tumor is encapsulated by a thick fibrous connective tissue. Portions may extend into the salivary tissue. This makes removal difficult and the margins unclear.	The facial nerve may be involved and careful removal of the tumor needs to be performed. The entire salivary gland may need removal in some cases.	Follow-up and monitoring are crucial since recurrence is possible.

continues

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Papillary cystadenoma lymphomatosum (Warthin tumor)	Warthin tumor is the second most common benign salivary gland tumor.	Salivary ducts embedded in lymph nodes during embryogenesis is one theory and smoking has been associated with this tumor as well. Damage to the DNA in the cells of the parotid gland may initiate the neoplastic process. Environmental agents are implicated.	These tumors are slow-growing, rubbery or firm, painless masses and usually found at the tail of the parotid gland near the angle of the mandible. The patient may complain of pain, tinnitus, and deafness, depending upon the size of the growth.	Microscopically, cystic spaces contain papillary projections that are lined by columnar cells supported by underlying layers of lymphoid tissue.	Extraoral palpations are needed to detect any tumor. The tumor is often bilateral. These tumors have decreased as smoking cessation has occurred with many patients. Removal may damage nerves and cause Frey syndrome.	Smoking cessation is crucial in discouraging these tumors. Dental practitioners should mention the risk with these tumors to smokers. Close monitoring and follow-up are needed.
Mucoepidermoid carcinoma	Unknown	Tumors are thought to arise from proliferation of undifferentiated excretory stem cells. Proliferation may be caused by inactivation of tumor suppressor genes or deletion of chromosomal material.	The tumor is described as a painless swelling. It may be present for years before being noticed by a health care provider. As growth continues, the symptoms reported by the patient seem to increase.	Radiographically, these may appear as a unilocular or multilocular growth. Microscopically, the lesion is composed of a combination of mucus-secreting cells and epidermoid cells. The tumors exhibit varying degrees of aggressiveness from low grade to high grade. The more aggressive tumors have fewer mucus-secreting cells.	Surgical removal is needed. The surgery depends upon the size of the tumor as to how much tissue will be removed. High-grade tumors usually warrant postsurgical radiation. The higher the grade of the tumor, the lower the prognosis.	Palpation of all major salivary glands should occur. The tumor is usually present for several years before being detected by dental professionals.
Acinic cell carcinoma	True etiology is not known. The parotid gland is most often affected followed by the submandibular glands and then minor salivary glands.	Acinic cell carcinomas arise from serous cells within the major salivary glands. Mutations in DNA are thought to initiate the process.	Present as slow-growing hard masses in the parotid and submandibular glands. Facial paralysis occurs infrequently but indicates a less favorable prognosis. When occurring in minor salivary glands, favored areas are on the palate, buccal mucosa, or lips.	The microscopic presentation can be highly variable. A biopsy is needed to determine the type of salivary tumor.	The chance of recurrence is high. The entire submandibular gland is removed when a tumor is found in this area. Adequate margins must be obtained. The prognosis is good, but local recurrence and metastasis are possible.	Dental professionals often find the tumors during a routine exam. The intraoral and extraoral exam with palpation is very important in tumor detection.
Polymorphous low-grade adenocarcinoma (PLGA)	Genetic mutation and the overproduction of specific gene products including the protein p63	Proliferation of salivary duct cells	The palate is the most common site. The growth presents as a slow-growing, painless mass that may be present for years. Usually in patients over age 40.	Ductal cells of this neoplasm display different growth patterns, hence the name polymorphous.	Surgical excision with possible local recurrence. Metastasis is uncommon.	One of the first signs of this neoplasm may be a denture that starts to feel uncomfortable or loose. This is an important reason to encourage denture patients to have a good exam.
Adenoid cystic carcinoma	Genetic mutation is noted.	This is a high-grade malignancy. Occurs most frequently in the minor salivary glands followed by the parotid and submandibular glands.	Most ACCs occur in the 40- to 60-year-old range with equal male/female distribution. This is a nonencapsulated tumor. The tumor is a well-defined mass within the gland. The mucosal surface may be ulcerated. The palatal growth may cause destruction of the bone and the patient will report pain.	Composed of cystic spaces and clusters of cells that form duct-like structures. Nerve fibers are usually invaded.	Radiation therapy is performed and there is a need to have all dental work completed prior to the surgery and radiation treatment. The facial nerve is often sacrificed.	Xerostomia and the oral side effects of radiation treatment are the prime concerns. Close follow-up and monitoring are needed.
Neurofibromatosis, type 1 (von Recklinghausen disease of the skin)	Mutation of the NF1 gene on chromosome 17. All ethnic groups are affected and equal male/female is reported.	Neurofibromin is a substance that functions as a tumor suppressor and subjects are deficient in this substance.	Clinically, the person appears with multiple neurofibromas, café au lait macules, Lisch nodules, a short stature, seizures, hypertension, and learning disabilities.	They are composed of spindle cells in a delicate connective tissue matrix. Mass cells are usually present.	There may be impairment of mastication, swallowing, and speaking. Lesions in the plane of occlusion become ulcerated. Home care modification must be made to assist the patient in home care.	The patient should be monitored and careful consultation with the patient's physician is needed.

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Multiple endocrine neoplasia (MEN) 2B	MEN refers to a group (types 1, 2A, and 2B) of rare and aggressive forms of a genetic disorder. Conditions characterized by hyperplasia of neuroendocrine origin. These are associated with multiple mucosal neuroma syndromes and classified as type 2B.	May be inherited as an autosomal dominant trait or can occur spontaneously as a new mutation. Mutation and activation of the RET protooncogene cause hyperplasia of the target cells located in the thyroid and adrenal glands as well as the mucosal tissues.	Mucosal neuromas can be found on the lips, tongue, and any other oral mucosal surface. The tongue is a common location. These are usually early signs of the MEN 2B. Individuals have a tall, slender body with long arms and referred to as a marfanoid body type. Increases of thyroid cancer and adrenal gland tumors are seen in these patients.	Mucosal neuromas display marked hyperplasia of nerve bundles in loose connective tissue.	The importance of early detection cannot be emphasized enough. Routine oral examination and palpation are needed to detect nodules and close examination of the oral structures is crucial.	The prognosis is good if the disease is identified early and the thyroid is prophylactically removed. If medullary carcinoma of the thyroid is present, there is a poor survival rate of 5 years at about 50%.
Lymphangioma	Etiology is unknown but a genetic tendency is suspected.	Lymphangioma is thought to be a congenital malformation of lymphatic vessels associated with islands of misplaced embryologic lymph tissue that develop independently of the lymph system.	The most common location is the head and neck. Cystic hygroma affects the neck and submandibular spaces. Cystic hygromas cause respiratory obstruction and are life threatening. The growths get larger with trauma and infection that results in inflammatory response.	The lesion is composed of endothelial-lined walled channels that are found just beneath the epithelial surface.	Laser surgery is sometimes appropriate in some cases and sclerotherapy as well.	The prognosis for small, isolated lesions is excellent. The larger lesions and cystic hygroma are based on location and size of the lesions. Complications from surgery occur frequently. Patients who have had surgical removal of the lymphangioma may have damage to the tongue and may be difficult to manage.
Cervical lymphoepithelial cyst (branchial cleft cyst)	Usually occur in the lateral cervical region but may develop in the parotid gland	Parotid gland epithelium becomes entrapped within the cervical lymph nodes. The cyst enlarges as the epithelial cells proliferate.	Usually found along the anterior border of the sternocleidomastoid muscle. It is soft and fluctuant when palpated. An abscess within the cyst is sometimes discovered. The counterpart to this cyst when found intraorally is the lymphoepithelial cyst found on the floor of the mouth.	Composed of stratified squamous and/or pseudostratified columnar epithelium supported by connective tissue containing lymphoid cells	Complete surgical excision is needed.	Untreated growths lead to recurrent infections and abscesses. Good recall maintenance and monitoring are needed. Providing good intraoral and extraoral examination with palpation is crucial in detecting any abnormalities at an early stage.
Thyroglossal tract cyst (thyroglossal duct cyst)	Most common of the developmental cysts and seen more often in children. Due to failure of obliteration of the thyroglossal duct that forms a bridge between the base of the tongue and the thyroid gland.	The cyst originates in the embryologic development of the thyroid gland. Immature thyroid tissue migrates down an epithelial duct or tract to its permanent location at the level of the thyroid cartilage at about 7 weeks in utero. This epithelium usually undergoes atrophy; sometimes remnants remain and undergo proliferation leading to this growth.	Fluctuant mass seen in the midline of the neck. Patients may report pain, dyspnea (shortness of breath), dysphagia (difficulty in swallowing), and discharge. However, in most cases, the growth is asymptomatic.	Central cavity lined by stratified squamous columnar and/or cuboidal cells. Some cysts do contain evident thyroid tissues.	A clear diagnosis should be made before any attempt to remove the cyst since the only thyroid tissue may be within the growth. Surgical removal is the treatment of choice long-term.	Careful follow-up and maintenance. Prognosis is excellent with complete removal.
Dermoid cyst	Uncommon cyst that is located in the midline of the head and neck. Result from entrapment of epithelial cells along the lines of embryonic closure or fusion.	The traces of epithelium trapped in embryonic lines of fusion may proliferate and lead to the epithelial-lined cavity.	The cyst develops as a painless, slow-growing, soft, doughy, midline mass. This cyst can be more obvious in the floor of the mouth or inferior to the muscles appearing as a swelling in the neck region.	Displays a central cavity lined by orthokeratotic squamous cell epithelium supported by a connective tissue wall containing sebaceous glands, sweat glands, and hair follicles. Large amounts of keratin and sebum from the glands in the connective tissue wall fill the cavity.	Surgical excision and biopsy	If the cyst is evident in the floor of the mouth, it can impair swallowing, speaking, and chewing. There is a slight chance of malignant transformation in dermoid cysts that have been present for a long time.

CHAPTER 18

Hard Tissue Enlargements

KEY TERMS

Ameloblastoma
Calcifying epithelial odontogenic tumor
Cementoossifying fibroma
Central giant cell granuloma
Chondroma
Chondrosarcoma
Chronic osteomyelitis with proliferative periostitis
Dysesthesia
Ewing sarcoma
Exostosis/exostoses
Liesegang rings
Mandibular tori (sing., mandibular torus)
Neoperiostosis
Odontogenic tumor
Ossifying fibroma
Osteosarcoma
Parosteal osteosarcoma
Pindborg tumor
Subpontic osseous proliferation
Torus palatinus

LEARNING OUTCOMES

1. Use and define the key terms listed in this chapter.
2. Name three areas in which bony growths may occur in the mouth and state the correct term for each growth of bone.
3. List the types of osteomyelitis that may occur in the oral tissues.
4. State the etiology of the ameloblastoma.
5. Compare and differentiate between the calcifying epithelial odontogenic tumor (CEOT) and the ameloblastoma.
6. Describe the clinical and radiographic characteristics of the osteosarcoma.
7. List the radiographic characteristics of the central giant cell granuloma (CGCG) and the clinical signs that would suggest such a lesion.
8. Describe the radiographic appearance of the osteosarcoma, chondrosarcoma, and Ewing sarcoma.
9. Describe three of the clinical signs that may be associated with each of the following: osteosarcoma, chondrosarcoma, and Ewing sarcoma.

CHAPTER OUTLINE

Variations of Normal
- Torus palatinus and/or mandibular tori
- Exostosis

Infections
- Chronic osteomyelitis with proliferative periostitis

Neoplasms
- Ameloblastoma
- Calcifying epithelial odontogenic tumor
- Ossifying fibroma
- Central giant cell granuloma
- Osteosarcoma
- Chondrosarcoma
- Ewing sarcoma

RELATED CLINICAL PROTOCOLS

#11 Patient Education: Oral Cancer Self-Examination
#12 Adjunctive Oral Premalignant Screening Devices
#14 Postoperative Instructions for Oral Surgery Patients
#19 Oral Health Care Management of the Patient with Cancer
#25 How to Utilize Nutritional Counseling in Practice
#26 Helping Relationships for Dental Hygienists

Hard tissue enlargements are found periodically in the mouth and must be evaluated to determine whether there is pathology. Some are benign, and others are malignant. The suffix "oma" refers to a tumor or neoplasm, as discussed in Chapter 5. The prefix "osteo" (bone forming), added to the root word "sarcoma" (neoplasm of connective tissue) is one example of the various word forms that are joined together to name a disease. Osteosarcoma, discussed later in this chapter, is a malignant neoplasm of connective tissue that is considered very aggressive. Common types of hard tissue enlargements such as the torus palatinus, mandibular torus, and exostosis are benign lesions. Other enlargements such as the sarcoma-type lesions and those that cause expansion with tissue destruction such as the ameloblastoma are discussed in this chapter. Other than the torus palatinus, mandibular torus, and exostoses that are almost always confirmed clinically, the diagnoses of many other lesions must be confirmed by directly viewing their cells under the microscope. In other instances, radiographs or special tests may be needed to determine the etiology of the lesion. This chapter discusses the types of hard tissue lesions the practitioner may consider in clinical evaluations.

Variations of Normal

These lesions find their origin from the bone and have a firm to hard texture. Three benign findings—the **mandibular tori**, the **torus palatinus**, and general exostosis—are detailed in this section. Occasionally, these growths of bone exhibit an unusual clinical presentation, in which case, biopsy or other tests may be needed to ensure a correct diagnosis. However, for the most part, these growths are very evident clinically and can be easily diagnosed.

NAME: Torus palatinus and/or mandibular torus

Etiology: Both of these conditions appear to be associated with a genetic and ethnic predisposition for their development. In addition, masticatory stresses from bruxing and clenching have been suggested as contributing factors in their etiology. Environmental factors related to injuries, such as burns and blunt force trauma affecting the bone, have also been implicated.

Method of Transmission: Not applicable

Epidemiology: The growths are usually found in adults and occur after puberty. There is a female predilection of 2:1 for the torus palatinus, but mandibular tori are reported to occur more frequently in males. The palatal growth is found in higher numbers of Asians, Eskimos, Japanese, and Native Americans. The appearance of tori is reported to be more common in Mongols (Garcia-Garcia, 2010). Studies by Al Quran (2006) examined 338 patients in Jordan. The researchers reported that 13.9% of the study participants had tori. The highest prevalence was for mandibular tori, with 20 of 47 study participants having bony growths in the mandible. Torus palatinus was slightly less common (14 of the 47 participants). A larger Turkish study of schoolchildren (Yildiz, 2005) reported a group of 1,943 children from age 5 to 15 years. The prevalence rate was 30.9%, and torus palatinus was significantly more frequent in females than in males. Depending upon the region of the world and the ethnicity of the population, the prevalence varies considerably. Reports in the United States place the prevalence rates for torus palatinus at a much higher rate of up to 25% and the mandibular tori at a slightly lower rate of about 10 to 12%.

Pathogenesis: Curran et al. (1999) reports a mother, daughter, and grandmother who all had autosomal dominant osteosclerosis, mandibular tori, and palatine tori. Genetic predisposition is the most widely accepted theory. Other theories include injury, parafunctional habits, occlusal stress, and vitamin D consumption. The torus palatinus and mandibular tori comprise normal compact bone and usually appear after puberty and continue to enlarge throughout adulthood. Some lesions can become very large and may interfere with normal function.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: The torus palatinus is found in the midline of the hard palate where the growths may be large, lobulated, or in some cases, very subtle. In many cases, the elevation may not be apparent until the clinician palpates the area and notices a slight rise of elevation and firmness. The growths appear radiopaque on diagnostic radiographs because of the dense bone. Mandibular tori develop along the lingual aspect of the mandible and are usually bilateral, although occasionally they are unilateral.

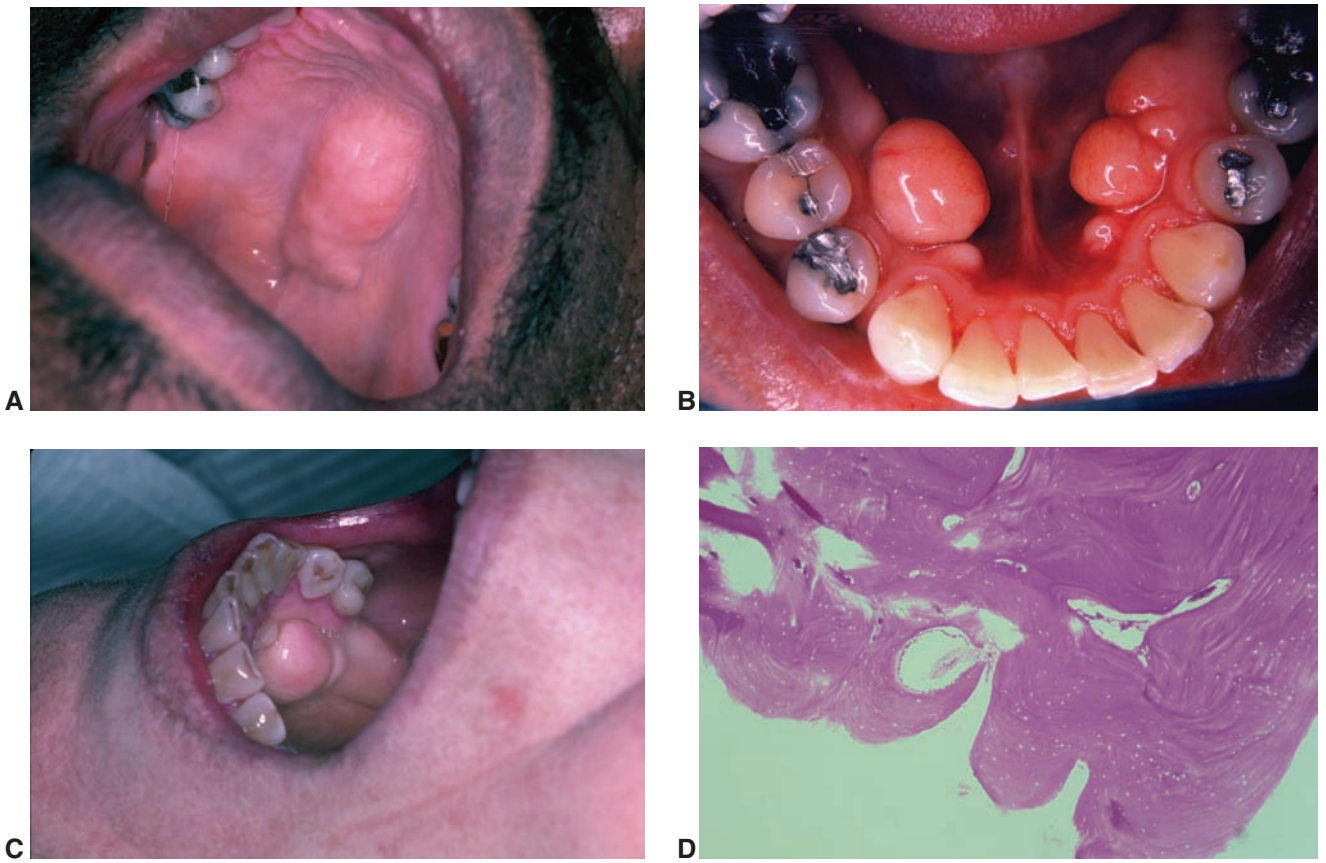


FIGURE 18.1. **A**. Torus palatinus. **B**. Mandibular tori. (Courtesy of Dr. Sumner Sapiro.) **C**. Mandibular tori. **D**. Histology of the torus.

Figure 18.1A depicts torus palatinus. Figure 18.1B shows mandibular tori (note the varying size of the mass of bone within the picture). Figure 18.1C depicts a mandibular torus that is more isolated to the right and middle of the mandible.

Distinguishing Characteristics: The location and clinical characteristics of these lesions are distinctive. In comparison to a tumor that would produce sudden and rapid growth, mandibular tori and the torus palatinus do not appear suddenly and do not grow rapidly.

Significant Microscopic Features: Mature, dense, lamellar cortical bone is characteristic of the histology seen in torus palatinus and mandibular tori. Figure 18.1D shows the histology of a torus palatinus demonstrating the dense, mature cortical bone of the specimen.

Dental Implications: Bony growths may interfere with speech, eating, and toothbrushing. On occasion, the growths may need to be removed for comfort and for the placement of dental appliances. The reasons for removal include: phonation, limitation in masticatory mechanics, inflammation, retention of food, prosthetic instability, and to use as a source for cortical bone grafts (Garcia-Garcia et al., 2010).

Differential Diagnosis: The torus palatinus and mandibular torus are usually diagnosed clinically because of their characteristic features and their location, unless they exhibit an uncommon appearance that may warrant further evaluation.

Treatment and Prognosis: The growths may become traumatized due to normal oral function. Standard treatment for this type of irritation is the same as for any other mucosal surface trauma. The growths normally pose no problem, and treatment is not usually needed.

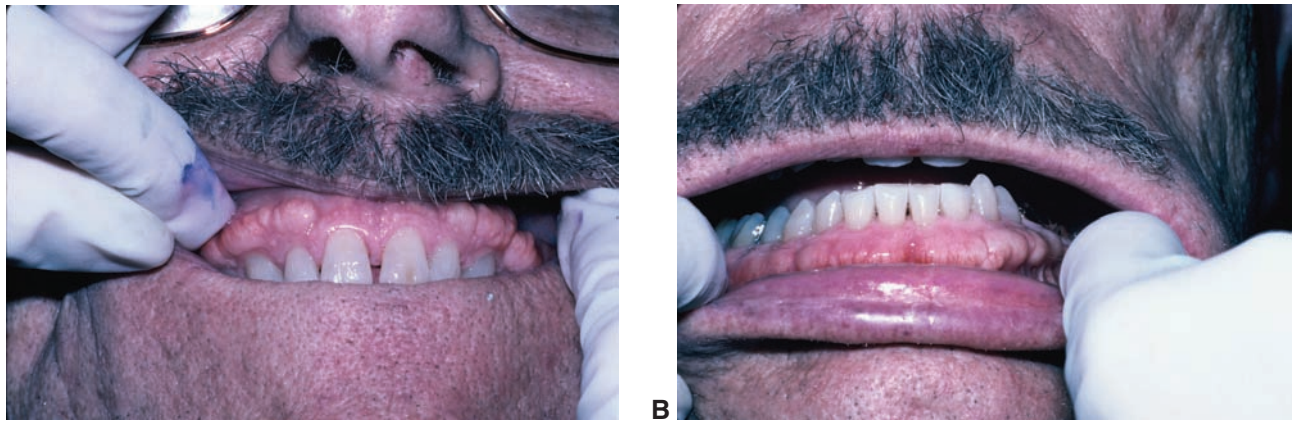
NAME: Exostosis

Etiology: **Exostosis** (pl., exostoses) represents an asymptomatic, exuberant growth of compact bone, occurring along the facial surfaces of the maxilla and the mandible. The growth can be single or may consist of multiple nodules composed of dense compact bone. The growth originates because of irritation and occlusal forces. Solitary exostosis is a single protuberance, usually due to frictional causes such as an ill-fitting dental prosthesis or bruxism.

Method of Transmission: Not applicable

Epidemiology: Exostosis occurs equally in males and females and is found more frequently in adults.

Pathogenesis: Exostosis has been reported in correlation with skin grafts, dental work such as bridges, and stressors, such as bruxism. Occasionally, a solitary bony growth may occur, usually in response to a local irritation factor.



18FIGURE 18.2. **A**. Maxillary exostosis. **B**. Mandibular exostosis.

The growths have been known to occur under the pontics of fixed bridges **(subpontic osseous proliferation**). The pontic replaces the missing tooth and has an open area under it, allowing the individual to clean the area more easily. In subpontic osseous proliferation, excess bone grows up into this opening, making oral hygiene procedures difficult (Burkes et al., 1985).

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: The bony growths tend to occur along the facial aspect of the maxilla and the mandible and manifest as lobulated, uneven solid bony growths. The posterior region is affected most often. The tissue appears a normal color unless the area has been traumatized. Figure 18.2A shows the multiple lobulated body growths in maxillary exostoses, and Figure 18.2B shows the multiple lobulated bony growths in mandibular exostoses.

Distinguishing Characteristics: The location and appearance of these lesions are characteristic.

Significant Microscopic Features: Mature hyperplastic cortical and trabecular bone are characteristic of the exostosis.

Dental Implications: It is important to determine if there are any direct causes associated with the development of the excess bone, such as bruxism. In this case, limiting excessive occlusal forces through the use of appliances or behavior modification would be optimal. Growths may need to be removed if dentures or other dental appliances are required.

Differential Diagnosis: The growths are usually diagnosed by their clinical appearance. Radiographs are sometimes helpful, especially in the case of a solitary exostosis, to rule out conditions that do not present as radiopaque lesions. Exostosis is a very hard, bony growth as are some malignancies. Some possible considerations of a solitary exostosis in a differential diagnosis are

1. Osteosarcoma, Chapter 18
2. Chondrosarcoma, Chapter 18
3. Ewing sarcoma, Chapter 18

Treatment and Prognosis: There is no treatment recommended for exostosis unless the growth interferes with dentures or there is continuous injury to the site producing chronic inflammation. If bruxism is a factor, night guards may be fabricated for the patient, to lower occlusal forces. Exostosis usually presents no problems and is left alone unless the area becomes highly irritated or other disease states are suspected.

Infections

Infections may occur throughout the body affecting many tissues and organs. The next section discusses the hard tissue enlargements that are caused by infection and produce changes in the bone and the surrounding tissues. One such broad category is osteomyelitis. Osteomyelitis is an inflammatory process of the bone and bone marrow caused by an infection. The initial infection is normally from a bacterial

APPLICATION 18.1

Exostosis may be very subtle, or patients may exhibit large areas of bony growths in both the maxillary and mandibular arches. Evaluating the patient for occlusion problems, bruxism, and stress-related clenching is part of a thorough oral examination. An evaluation of the patient's eating and sleeping patterns may give the clinician a good indication of whether the patient may be bruxing while sleeping and waking with tight or sore muscles. Determining bruxism early and providing a night guard can dramatically decrease the amount of damage that is occurring to the oral structures. Stress reduction and behavior modification techniques can be learned and greatly affect overall health in general. Unless a health care practitioner calls these conditions to the patient's attention, they often go unnoticed or undiagnosed and cause increasing problems.

source: staphylococci, streptococci, actinomyces, and other organisms. Abscesses, periodontal infections, jaw fractures, and cysts are often involved in the initiation of osteomyelitis. The condition can be acute or it may become chronic in the absence of treatment or the use of improper treatment. The difference between acute and chronic osteomyelitis is often related to the virulence of the bacteria involved. Acute osteomyelitis is always highly destructive. Several categories of chronic osteomyelitis exist, affecting different areas in the mouth. Chronic focal sclerosing osteomyelitis (condensing osteitis) is usually found as an area of radiodensity at the apex of a tooth, while diffuse sclerosing osteomyelitis exhibits more radiodensity throughout the jaw area. The bony sclerosis is a reaction to either an inflamed or a devitalized pulp, and the tooth will invariably be nonvital. Due to the radiographic appearances of the various forms of osteomyelitis, some lesions appear radiolucent while others appear radiopaque. Both chronic osteomyelitis and acute osteomyelitis are discussed in Chapter 20, "Radiolucent Lesions." Diffuse and focal sclerosing osteomyelitis is covered in Chapter 19, "Radiopaque Lesions." Chronic osteomyelitis with proliferative periostitis produces a hard, indurated, exophytic mass, and for this reason, it is discussed in this chapter.

NAME: Chronic osteomyelitis with proliferative periostitis (Garré osteomyelitis)

Etiology: **Chronic osteomyelitis with proliferative periostitis** is described as a proliferative inflammatory response of the periosteum to infection or other irritants. The lesion can originate from odontogenic factors, such as a periapical abscess or periodontal infection, or from nonodontogenic factors, such as bacteremia, oral surgery, or jaw fractures.

Method of Transmission: Not applicable

Epidemiology: Chronic osteomyelitis with proliferative periostitis is seen more often in children and young adults, with a mean age of 13 years; there is no sex predilection.

Pathogenesis: Chronic osteomyelitis with proliferative periostitis occurs when an infection, usually of odontogenic origin, passes through the cortex of the bone and involves the periosteum. The infection stimulates the periosteum to become hyperplastic and causes the body to lay down bone on the surface of the cortical bone to wall off the infection, which results in enlargement of the bone. This type of bone growth produces a characteristic layering of bone (onionskin pattern) that is observed on the surface of the cortical bone on a radiograph. This onionskin effect is also referred to as **neoperiostosis** (described by Eversole et al., 1979).

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: The lesion appears as an asymptomatic, unilateral, bony, hard protuberance with normal tissue covering the growth. It usually involves the posterior regions of the mandible. Radiographs of the lesion show evidence of neoperiostosis. Figure 18.3 depicts proliferative periostitis in an 8-year-old boy. The image on the left was taken at the initial examination and shows the classic appearance of neoperiostosis or onionskin pattern. The image on the right was taken 12 months later, after endodontic therapy, and shows resolution of the lesion. The initial diagnosis was pulpal necrosis with a provisional diagnosis of chronic osteomyelitis with proliferative periostitis. The bony enlargement of 3 to 4 cm in diameter and 1.5 cm in depth is evident on the radiograph.

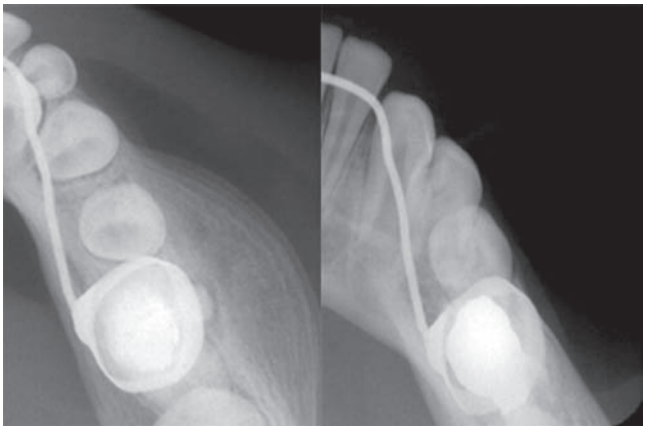


FIGURE 18.3. Proliferative periostitis. (Courtesy of Dr. J. Craig Baumgartner.)

Distinguishing Characteristics: The onionskin pattern of the bone growth, presence of a dental infection, and young age of the patient are characteristic features of this condition.

Significant Microscopic Features: The microscopic appearance is that of newly formed bone consisting of osteoid and primitive bone in a fibrous connective tissue stroma that is scantily infiltrated by lymphocytes and plasma cells. The vital bone is oriented perpendicular to the surface epithelium.

Dental Implications: Tooth mobility may be a problem, depending upon the degree of advancement and stage of treatment related to chronic osteomyelitis with proliferative periostitis. The source of the irritation must be removed. Endodontic treatment has been successful in some cases, but extraction of the tooth may be necessary in other situations.

Differential Diagnosis: Neoperiostosis also occurs in the following conditions, which should be considered in the differential diagnosis:

1. Ewing sarcoma, Chapter 18
2. Osteogenic sarcoma, Chapter 18
3. Congenital syphilis, Chapter 12
4. Fluorosis, Chapter 21

Treatment and Prognosis: The treatment protocol for chronic osteomyelitis with proliferative periostitis is the identification of the bacteria involved and subsequent removal of the tooth or teeth or endodontic treatment in the area affected. The use of antibiotics is often required as part of the course of treatment. The prognosis is good, and the bone will resolve over time. Osteomyelitis is further discussed in Chapter 19.

Neoplasms

Neoplasms are new growths of tissue that may be either benign or malignant. Neoplasms provide no benefit to the host. The lesion or tumor will continue to expand and grow even after any known stimulus is removed (see Chapter 5). The following section discusses neoplasms that appear as firm or hard nodules in the mouth.

NAME: Ameloblastoma

Etiology: The **ameloblastoma** is classified as an **odontogenic tumor**. Odontogenic tumors arise from epithelial or mesenchymal remnants of tooth-forming tissues, such as the remnants of the rests of the enamel organ, dental lamina, Hertwig sheath, the rests of Malassez, rest of Serres, or the reduced-enamel epithelium. They may also be formed from the epithelial lining of an odontogenic cyst, such as the dentigerous cyst (see Chapter 20).

Method of Transmission: Not applicable

Epidemiology: Ameloblastomas are the most commonly occurring odontogenic tumors. Several varieties exist with individual histological characteristics. Most occur in adults from 20 to 50 years of age, predominately in the fourth and fifth decades. The median age is approximately 35 years old (Mendenhall et al., 2007). There is no sex predilection. Approximately 80% occur in the mandibular molar region around impacted third molars, reaching the angle of the mandible. The tumor can occur in the maxilla as well.

Pathogenesis: The ameloblastoma presents as a multilocular or unilocular lesion composed of epithelial cells. There are several types of ameloblastoma, including follicular, plexiform, desmoplastic, acanthomatous, basal cell, granular cell, and peripheral. Ameloblastomas may also be extraosseous, but these are very rare. Malignancy is also rare, occurring in less than 1% of all ameloblastomas. Normally, ameloblastomas are considered benign growths, even though they are locally aggressive, invasive, and expansive.

Extraoral Characteristics: The expanding ameloblastoma may cause facial asymmetry, which might be the first indication that a tumor exists. Until discovered on radiographs, the lesions are usually asymptomatic.

Perioral and Intraoral Characteristics: The ameloblastoma appears as a painless swelling, usually in the posterior mandibular region. Buccal and lingual expansion in the area is frequently present upon clinical examination. The ameloblastoma may cause root resorption, and teeth may become mobile as the neoplasm expands. When viewed on a radiograph, ameloblastomas appear as multilocular and sometimes unilocular radiolucencies with well-defined, scalloped margins. The multilocular lesions exhibit a characteristic "soap-bubble" when large and a "honeycomb" appearance when small. Figure 18.4A shows a radiograph of an ameloblastoma in the left mandibular region. Note the multilocular appearance of the lesion. Figure 18.4B depicts an ameloblastoma in the mandibular molar region.

Distinguishing Characteristics: The "soap-bubble" radiographic appearance and well-defined scalloped margins are characteristic features of this lesion.

Significant Microscopic Features: The ameloblastoma appears as palisading columnar cells around epithelial nests resembling the enamel organ. Elements of the stellate reticulum of the enamel organ are present. Depending upon the type of ameloblastoma, there may be nests of tumor cells or tumor islands. Peripheral cells resemble ameloblasts with reverse polarity of their nuclei. The islands resemble the stellate reticulum of the enamel organ. The lesion is not encapsulated but invades wide areas of tissue when left to grow. Figure 18.4C depicts the histology of an acanthomatous-type ameloblastoma. Note the labeled appearance of the ameloblast-like cells and the appearance of stellate reticulum-like areas noted on the slide. Peripheral cells resemble ameloblasts with reverse polarity of their nuclei. The islands resemble the stellate reticulum of the enamel organ.

Dental Implications: Although the ameloblastoma is a localized nonencapsulated lesion, it can break through the cranial cavity by expansion, making it life threatening. When ameloblastomas are discovered in the maxilla, they can result in death due to direct extension into vital structures. The lesions also become more difficult to manage when they spread through the bone into the soft tissues.

Differential Diagnosis: Differentiation of this lesion from cysts and other radiolucent lesions is required and is determined through biopsy. Any of the tumors that exhibit a multilocular or unilateral appearance on radiographs should be considered, such as:

1. Calcifying epithelial odontogenic tumor, Chapter 18
2. Odontogenic myxoma, Chapter 20
3. Dentigerous cyst, Chapter 20
4. Odontogenic keratocyst, Chapter 20
5. Central giant cell granuloma, Chapter 18
6. Ossifying fibroma, Chapter 18

The only way to obtain a definitive diagnosis of any of these lesions is through biopsy.

Treatment and Prognosis: Excision is the course of action. The tumor requires wide excision with clear margins to lessen the chance of recurrence. Careful radiographic follow-up is necessary to ensure early detection of any recurrence. The prognosis is good when timely treatment is rendered, but ameloblastomas may recur, and untreated ameloblastomas can result in death.

NAME: Calcifying epithelial odontogenic tumor (CEOT) (Pindborg tumor)

Etiology: The **calcifying epithelial odontogenic tumor (CEOT),** or **Pindborg tumor** (Pindborg, 1955), is an odontogenic tumor probably originating from remnants of the enamel

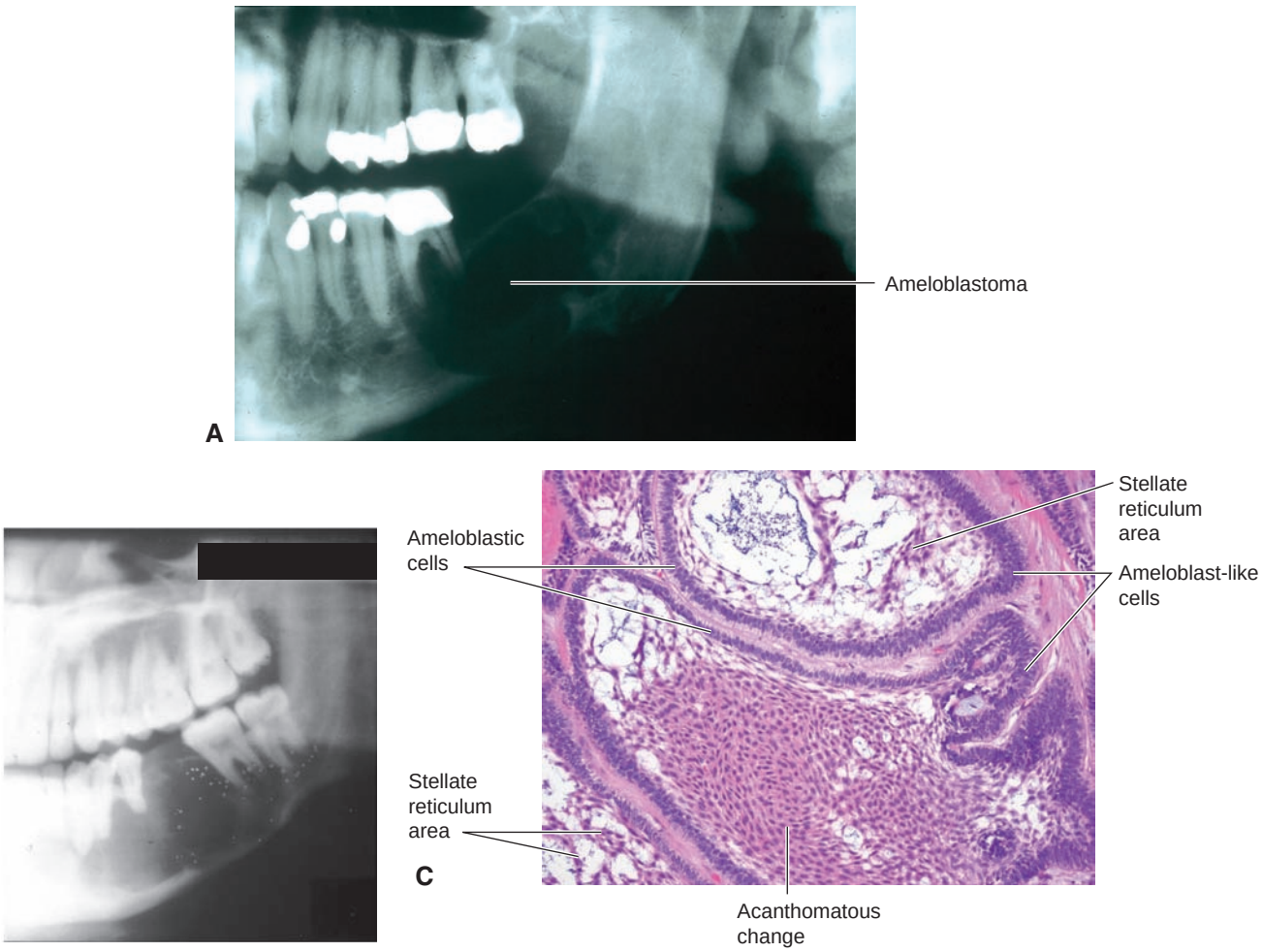


FIGURE 18.4. **A**. Ameloblastoma intraoral. (Courtesy of Dr. John Jacoway.) **B**. Ameloblastoma. (Courtesy of Dr. John Jacoway.) **C**. Ameloblastoma histology. (Courtesy of Dr. Harvey Kessler.)

organ. Although the precise origin is not known, it is associated with unerupted teeth. Some believe it to be derived from the stratum intermedium layer of the enamel organ and others believe that it arises from the remnant of the dental lamina.

Method of Transmission: Not applicable

Epidemiology: The CEOT can occur in any age group, but is usually found in 20- to 50-year-olds; it occurs equally in males and females. The CEOT accounts for about 1% of all odontogenic tumors and occurs less frequently than the ameloblastoma (Singh et al., 2011). The mandible is affected twice as often as the maxilla. Peripheral (extraosseous) odontogenic tumors are rare, with recent reports in the United States of 2.2% reported to be CEOTs.

Pathogenesis: The CEOT is a benign, slow growing, but locally invasive tumor, occurring in both intraosseous (94%) and extraosseous (6%) sites. Reports in the literature present some isolated malignant transformations (Zhong et al., 2010). This lesion is much less aggressive than the ameloblastoma, but like the ameloblastoma, the CEOT is locally invasive. It is well encapsulated and usually a round- to ovoid-shaped mass (Angadi & Rekha, 2011).

External Characteristics: A large CEOT may produce clinically observable facial asymmetry resulting from expansion of the jaw.

Perioral and Intraoral Characteristics: The CEOT manifests as a slow-growing, painless jaw expansion, usually in the molar and premolar region of the mandible. A maxillary CEOT tends to grow more rapidly than one in the mandible and does not remain as well confined. These lesions are often associated with impacted teeth. The intraosseous usually involves the mandible primarily in the molar/premolar region while the extraosseous variant involves the anterior gingival region. Radiographically, the CEOT appears as a multilocular radiolucent lesion with variable amounts of calcification. Figure 18.5A is a radiograph of a CEOT with diffuse opaque calcifications in the crown region of the unerupted lower right third molar.

Distinguishing Characteristics: A distinct entity, referred to as **Liesegang rings**, may be visible microscopically when calcification within the CEOT is dense enough (Raso et al., 1998). The rings represent calcified deposits forming within the tumor islands of the specimen. Figure 18.5B depicts the histology of a CEOT and shows a closer view of the Liesegang rings.

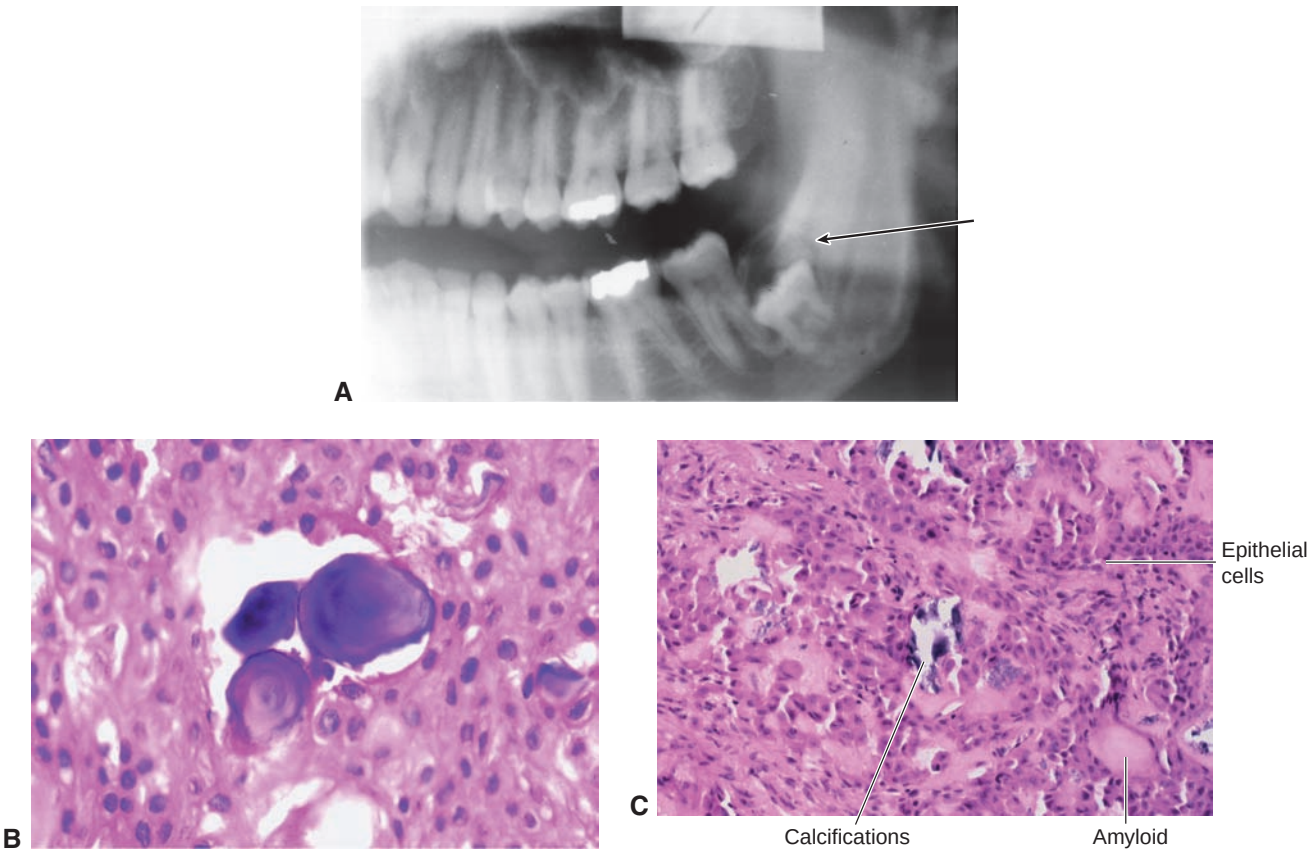


FIGURE 18.5. **A**. Calcifying epithelial odontogenic tumor (CEOT). (Courtesy of Dr. Harvey Kessler.) **B**. CEOT histology depicting Liesegang rings. (Courtesy of Dr. Harvey Kessler.) **C**. CEOT histology. (Courtesy of Dr. John Jacoway.)

Significant Microscopic Features: The CEOT is made up of islands and sheets of polyhedral epithelial cells in a non-inflamed connective tissue stroma. Deposits of hyaline (enamel protein) that resemble amyloid-like material are components of the CEOT. Figure 18.5C depicts the histology of a CEOT with areas of hyaline (amyloid), epithelial cells, clumps of polyhedral tumor cells with indistinct borders, and some calcifications.

Dental Implications: These tumors are usually discovered when the patient notices and reports facial asymmetry or they are diagnosed during a routine radiographic examination. The potential of identifying lesions such as this emphasizes the need for periodic clinical and radiographic dental evaluations. The patient should be followed closely for any sign of recurrence.

Differential Diagnosis: Since the CEOT may be radiolucent or may contain foci of calcification, the differential diagnosis is sometimes not readily apparent. In addition to cysts, fibromas, and tumors, the following are considerations:

1. Odontogenic keratocyst, Chapter 20
2. Dentigerous cysts, Chapter 20
3. Ameloblastoma, Chapter 18
4. Adenomatoid odontogenic tumor, Chapter 20
5. Calcifying odontogenic cyst, Chapter 20
6. Odontoma, Chapter 19

Treatment and Prognosis: Surgical removal of the tumor with a wide margin of normal tissue is the required procedure. The prognosis is excellent. A recurrence rate of 10 to 20% following conservative treatment is reported (Neeraj et al., 2011).

NAME: Ossifying fibroma (cementoossifying fibroma)

Etiology: The **ossifying fibroma**, or **cementoossifying fibroma,** is a benign neoplasm, composed of cementum-like calcifications and bony components. The cause is not known. The ossifying fibroma is considered one of the bone lesions of a collection of "fibro-osseous lesions" of bone (Ram et al., 2012).

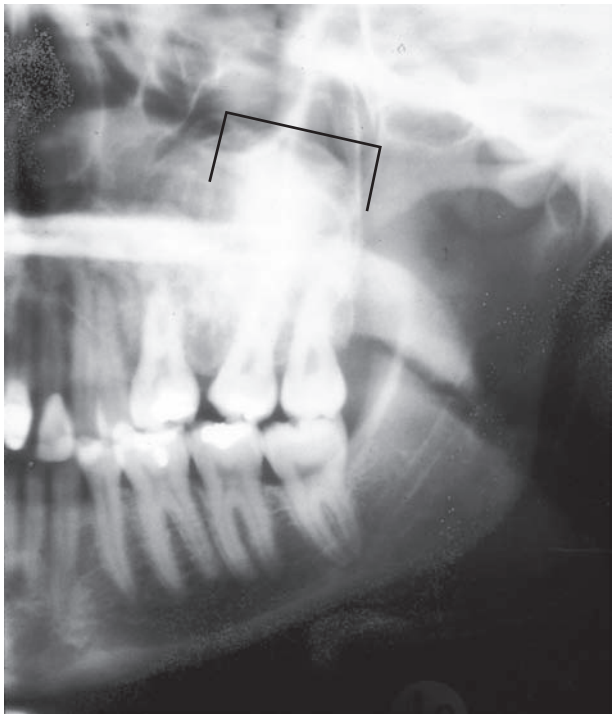
Method of Transmission: Not applicable

Epidemiology: The ossifying fibroma occurs most commonly in the third and fourth decades of life. This lesion generally occurs in the premolar and molar regions of the mandible. There is a high female predilection of 5 to 1.

Pathogenesis: The pathogenesis is not known but there may be a genetic component.

Extraoral Characteristics: Larger ossifying fibromas may cause swelling and facial asymmetry.

Perioral and Intraoral Characteristics: Ossifying fibromas are most often slow growing, painless, and expansile. The larger versions of this lesion may appear as a nonpainful swelling. Otherwise, the lesion may be clinically undetectable but



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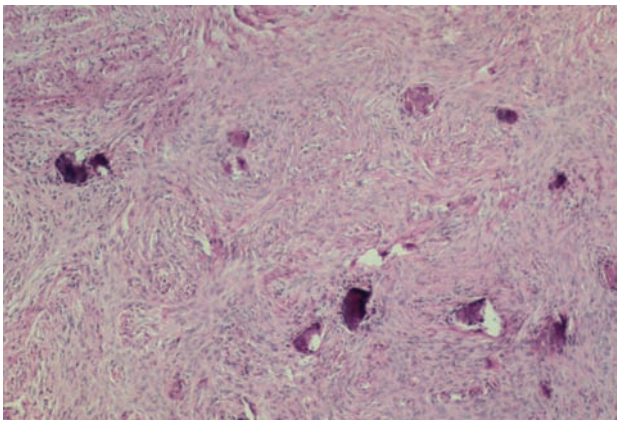


B

FIGURE 18.6. **A**. Cementoossifying fibroma radiograph. (Courtesy of Dr. John Jacoway.) **B**. Cementoossifying fibroma histology. (Courtesy of Dr. John Jacoway.)

may appear on a radiograph during a routine examination. The radiographic appearance is of a well-circumscribed radiolucency with variable density. Sclerotic borders may be evident in the radiograph, depending on the amount of calcification present. Root resorption or root divergence may be noted. The ossifying fibroma on the radiograph shown in Figure 18.6A clearly presents a radiopaque lesion at the apical area of the maxillary left molar region, with evident root divergence (diverging roots).

Distinguishing Characteristics: Radiographic lesions appear as well-defined, unilocular, radiolucent lesions with radiopaque calcifications. Diverging roots may be evident, or the lesion may appear dense and calcified.

Significant Microscopic Features: The histologic features appear as vascular, cellular, fibrous connective tissue with bone fragments that are both mature and immature. The collagen fibers are arranged in what is termed a "storiform pattern." The bone is immature, and osteoblasts are often seen. The tumor may be encapsulated, with fibrous tissue surrounding the perimeter of the lesion. Figure 18.6B depicts the histology of an ossifying fibroma, demonstrating the areas of calcified bony material within the specimen. The tissue specimen exhibits the storiform pattern that is characteristic of this type of lesion.

Dental Implications: The lesion is removed, and a complete diagnosis is made after the specimen is viewed microscopically.

Differential Diagnosis: The challenge with an ossifying fibroma is differentiating it from fibrous dysplasia (see Chapter 10), which is the primary entity in a differential diagnosis. The following are also considerations:

1. Focal cementoosseous dysplasia, Chapter 20
2. Focal osteomyelitis, Chapter 20

Treatment and Prognosis: Ossifying fibromas must be surgically removed. It is rare to have a recurrence, and they do not become malignant. The prognosis is excellent.

NAME: Central giant cell granuloma (CGCG)

Etiology: The **central giant cell granuloma** was, and in some areas still is, believed to be a reactive lesion or a reparative response to trauma or other local factors. However, many feel that because of its unpredictable and often aggressive nature it is a true neoplasm. This topic is controversial and is still being debated.

Method of Transmission: Not applicable

Epidemiology: The CGCG is considered a hard tissue enlargement accounting for fewer than 7% of all benign tumors of the jaws. There is a 65 to 75% prevalence for the mandible, where the CGCG is most often found anterior to the molar teeth and sometimes in the molar area. The ramus of the mandible is not a common site for the development of a CGCG. Although the lesion can appear at any age, it favors the under 20 age group, and there is a female predilection of 2:1. A study by Kruse-Losler et al. (2006) found 76.9% of study participants to be under the age of 30, with a female to male ratio of 1.8:1. Additionally, 69.2% of the lesions occurred in the mandible, with 57.7% appearing as unilocular lesions.

Pathogenesis: The CGCG lesion is usually discovered on radiographs, appearing as a radiolucent lesion with expanding margins. The first indication of the CGCG may be mobility or expansion of teeth. The lesions demonstrate aggressive behavior and are classified as neoplasms.

Extraoral Characteristics: While most cases occur within the maxilla and the mandible, CGCG can also affect small long bones, such as those of the hands and feet, and facial bones.

Perioral and Intraoral Characteristics: The lesion usually manifests as a painless expansion of the jaw, usually anterior to the first molar. If the lesion penetrates and protrudes through the cortical bone, it then appears as a soft tissue,

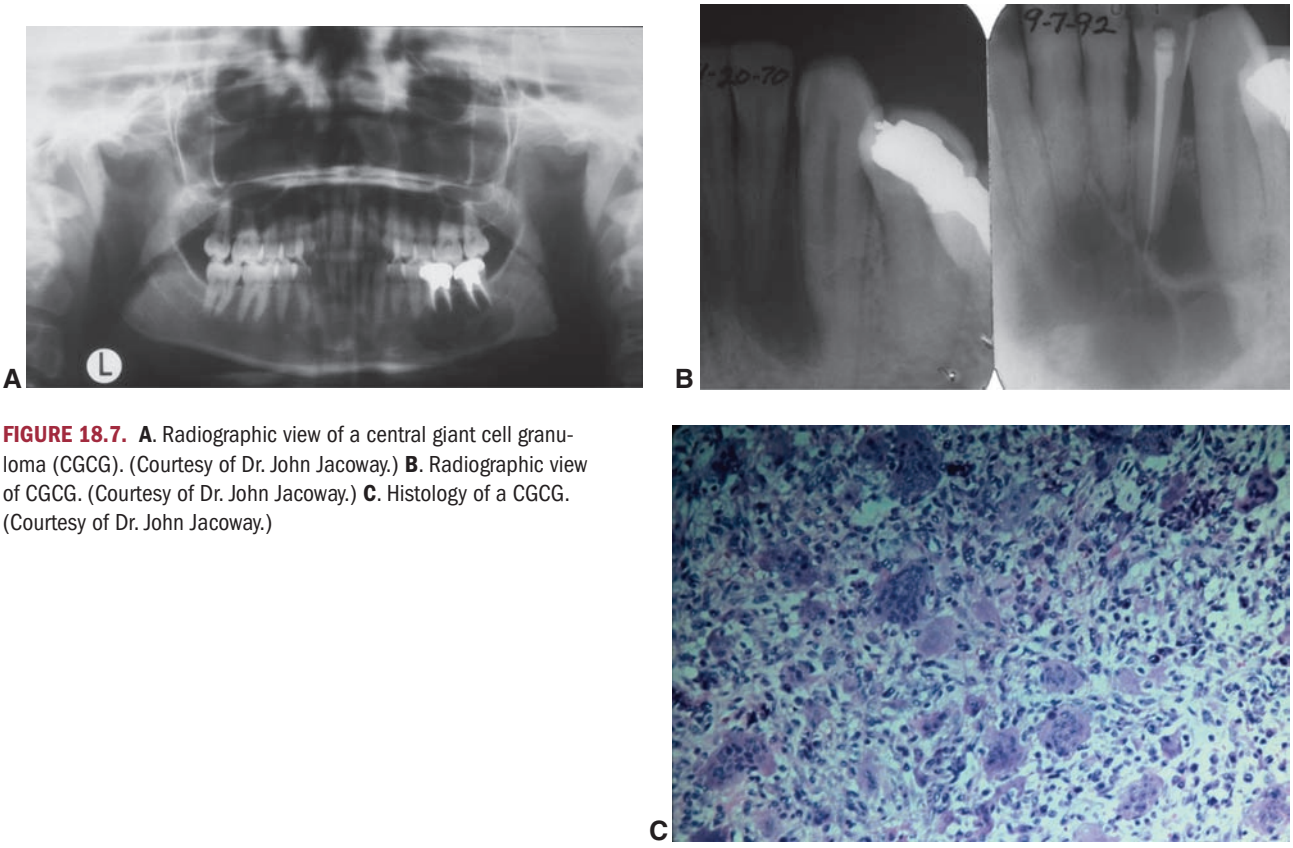


FIGURE 18.7. **A**. Radiographic view of a central giant cell granuloma (CGCG). (Courtesy of Dr. John Jacoway.) **B**. Radiographic view of CGCG. (Courtesy of Dr. John Jacoway.) **C**. Histology of a CGCG. (Courtesy of Dr. John Jacoway.)

flat-based nodule with a blue-to-purple color. There is usually no pain associated with the CGCG. The teeth may exhibit divergence. The radiographic appearance of the CGCG is of a radiolucent, multilocular, or less often unilocular lesion with scalloped and expanding margins. Figure 18.7A depicts a radiographic slide of a CGCG in the lower right mandibular region. Figure 18.7B shows a CGCG with a subsequent recurrence in the anterior region 22 years later.

Distinguishing Characteristics: The expansion of bone is a key feature of this lesion. The color variation of a blue-gray hue is sometimes a distinguishing characteristic for those patients who are seen clinically for perforation of the cortical bone plate.

Significant Microscopic Features: The lesion shows spindle-shaped mesenchymal cells with focal aggregates of small multinucleated giant cells. The stroma is that of fibroblast and fibrosis. Figure 18.7C shows the histology of a CGCG with multinucleated giant cells.

Dental Implications: Aggressive lesions may recur, and complete removal is indicated. The possibility of other systemic disease needs to be eliminated, and all factors evaluated. Hyperparathyroidism should be ruled out as well.

Differential Diagnosis: Tests may be needed to rule out other disorders that may be associated with the CGCG, such as bone cyst, fibrous dysplasia, chondroblastoma, and osteoid osteoma. It is difficult to differentiate between the CGCG and other multilocular lesions, such as early ameloblastomas. Additionally, in the early development, it is difficult to differentiate other lesions, such as the small focal cyst lesions. Other lesions to be considered are:

1. Hyperparathyroidism (Brown tumors), Chapter 7
2. Cherubism, Chapter 10
3. Giant cell tumors involving Paget disease, Chapter 10
4. Aneurysmal bone cysts, Chapter 19
5. Ameloblastoma, Chapter 18
6. Odontogenic keratocyst, Chapter 20

Treatment and Prognosis: Excision by curettage is the recommended treatment. A recurrence rate of 15 to 20% is noted. The more aggressive lesions tend to reoccur more often. Those occurring in children may have a higher rate of recurrence. The prognosis is good with complete removal.

NAME: Osteosarcoma (osteogenic sarcoma)

Etiology: **Osteosarcoma** is the most common primary malignant tumor found in bone and accounts for 20% of all bone tumors (McMains & Gourin, 2005). Gene tests find that mutations of the *Rb* gene and the *p53* gene are common in these neoplasms (see Chapter 5). In older persons, osteosarcoma is most often associated with Paget disease or past radiation exposure or chemotherapy for treatment of other diseases. Increased osteosarcomas have been found

in painters who at one time painted radium watch dials and wetted their brushes with saliva.

Method of Transmission: Not applicable

Epidemiology: This tumor accounts for about 25% of all sarcomas. Approximately 5 to 10% of all cases of skeletal osteosarcoma occur in the jaws (Takehana dos Santos, 2002). Osteosarcoma of the long bones, primarily the femur and tibia, most commonly occurs in the second decade age group and a decade later for osteosarcoma of the jaws, with the mean age being 35. Males are affected more often than females, with a predilection of 2:1. Worldwide, osteosarcomas affect about 1 per 100,000 persons per year. The mandible is affected more often than the maxilla, with most arising in the body of the mandible.

Pathogenesis: Although most osteosarcomas arise in the long bones, this sarcoma can be found in the maxilla and mandible. The mandible is more commonly affected, with the prime areas being the body, symphysis, and angle. A variant of osteosarcoma is **parosteal osteosarcoma**, a tumor that grows from the external surface of the bone. This type of osteosarcoma grows slowly and metastasizes late. The prognosis for this type is better than that for osteogenic sarcoma.

Extraoral Characteristics: Lung metastasis may occur with osteosarcoma.

Perioral and Intraoral Characteristics: The clinical symptoms may include pain, swelling, loose teeth, or numbness. **Dysesthesia** (a condition in which a disagreeable sensation is produced by ordinary stimuli) is also reported. Patients complaining of burning mouth syndrome often report unusual sensations that they have noticed, such as tingling and numbness in a specific area. In many cases of osteosarcoma, the radiographic appearance may be described as a "sunburst" pattern. When the neoplasm involves teeth, a widened periodontal ligament (PDL) space and root resorption (called "spiking resorption" because the roots have a tapered appearance) is observed. Figure 18.8A demonstrates the intraoral characteristics of an osteosarcoma in a 28-year-old white male. The tissue around teeth 19 and 20, as well as the distal retromolar, appears to be expansile. Figure 18.8B depicts the radiographic view of an osteosarcoma of the same patient, demonstrating the osteosarcoma on the left mandibular region with heavy bone growth in the molar region. Note the "sunburst" appearance of bone radiating around the inferior mandibular region. An obvious cystic structure is also present on the opposite side in the distal molar region of tooth 31–32 area. Figure 18.8C shows the sunburst appearance in significant detail in the

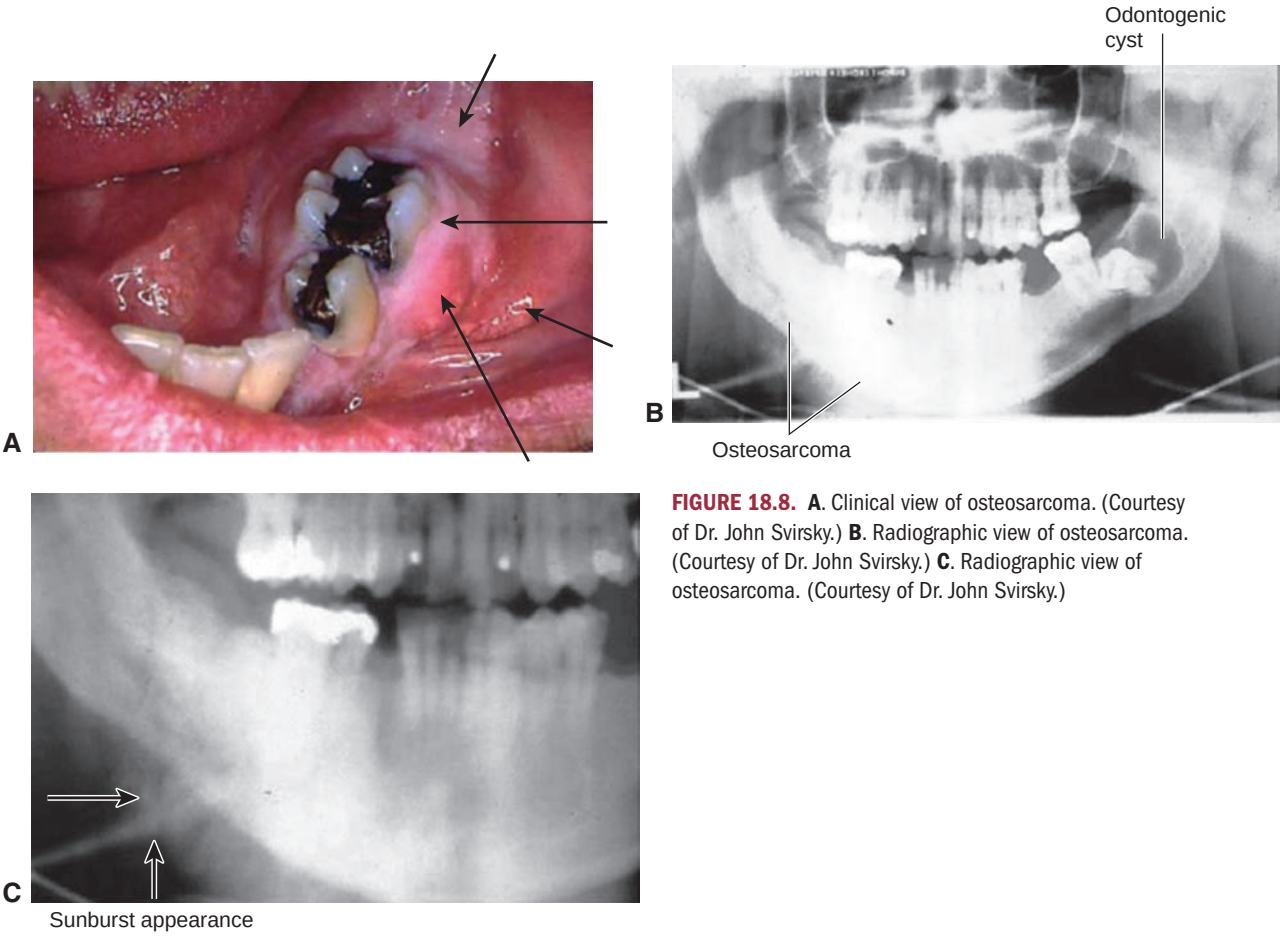
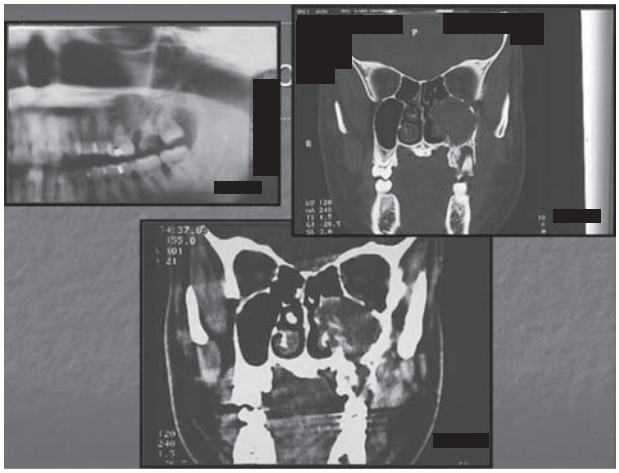


FIGURE 18.8. **A**. Clinical view of osteosarcoma. (Courtesy of Dr. John Svirsky.) **B**. Radiographic view of osteosarcoma. (Courtesy of Dr. John Svirsky.) **C**. Radiographic view of osteosarcoma. (Courtesy of Dr. John Svirsky.)



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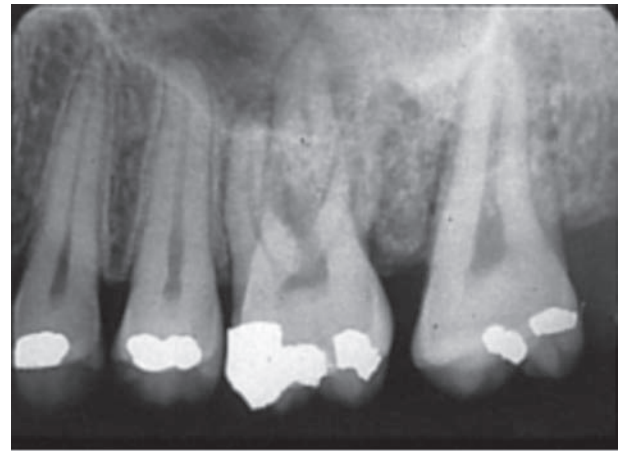


E

FIGURE 18.8. *(Continued)* **D**. Radiographic view, scans of osteosarcoma. (Courtesy of Dr. John Svirsky.) **E**. Radiographic view of osteosarcoma. (Courtesy of Dr. John W. Preece.)

same patient. Figure 18.8D depicts an osteosarcoma found in a 32-year-old male. View 1 represents the area on the upper left premolar region, with obvious destruction of the orbital floor. Views 2 and 3 show the scan with the tumor breaking through the left orbital area of the maxilla. Figure 18.8E represents the widening of the PDL in an osteosarcoma.

Distinguishing Characteristics: Symmetrical widening of the PDL of one or several teeth is often seen. Additionally, the typical "sunburst" or "spiking" seen radiographically are other distinguishing characteristics. Although other disease states may cause a widening of the PDL, osteosarcoma may be a strong consideration when pain and swelling have been reported.

Significant Microscopic Features: Pleomorphic malignant spindle cells, tumor giant cells, and mitoses are common features. The tumor produces bone matrix that is focally calcified. Also present are malignant cells producing osteoid. There is better differentiation of the osteosarcomas of the oral region than of the long bones such as the femur.

Dental Implications: The dental implications include tooth mobility, swelling, and pain. The patient may complain of nasal obstruction and paresthesia. The growth can affect the trigeminal nerve, causing paraesthesia. Fractures may be observed as well. Early radiographic evidence may be a widening of the PDL space as shown in Figure 18.8E.

Differential Diagnosis: CT scans and MRI techniques are needed to determine the extent of the lesion. Other neoplasms would be considered in the differential diagnosis depending upon the radiographic extent of the lesion and its radiolucent and radiopaque qualities. In addition, the following are also to be considered in the differential diagnosis:

1. Chronic osteomyelitis, Chapter 19
2. Metastatic carcinomas, Chapters 10 and 17
3. CEOT, Chapter 18
4. Chondrosarcoma, Chapter 18
5. Ewing sarcoma, Chapter 18

Treatment and Prognosis: Chemotherapy and surgical removal of the affected bone is the treatment of choice, with negative margins obtained around the periphery of the specimen. Poor rates of survival are correlated with the inability to obtain clear or negative margins during surgery. Survival varies, and reports are approximately 20% for 5 years, depending upon the extent of the lesion at the time of treatment.

NAME: Chondrosarcoma

Etiology: **Chondrosarcoma** is a malignant tumor of cartilage. There is some evidence of a genetic predisposition. Rarely, these tumors can form within preexisting benign chondromas. Postradiation chondrosarcoma has been seen in individuals receiving more than 7,000-rad dosages.

Epidemiology: Chondrosarcomas are much less common than osteosarcoma. Less than 1% of the chondrosarcomas found in the body are seen in the maxilla or the mandible. Chondrosarcomas arise in the third decade through the sixth decade of life, with most tumors reported to occur after the age of 40. A secondary form of chondrosarcoma occurs in younger patients between the ages of 20 and 40 years. Slightly more males are affected than females (ratio of 1.5 to 2:1). Chondrosarcoma is the second most frequently occurring primary sarcoma of bone, accounting for approximately 26% of all primary osseous sarcomas. Overall, 8 cases per 1 million population are reported (Hide, 2005).

Method of Transmission: Not applicable

Pathogenesis: Most chondrosarcomas arise in the pelvis, femur, ribs, and craniofacial bone. The presenting

features are not consistent, and reports of pain and no pain, with swelling and no swelling, appear to be equal. If untreated or inadequately treated, these lesions can become large and extend into vital structures, causing death. Metastasis to the lungs or other bones is more common in high-grade chondrosarcomas than in the lower grades.

Extraoral Characteristics: Depending upon the location of the chondrosarcoma and the extent of the lesion, external swelling and asymmetry may be visible due to the growth of the tumor.

Intraoral and Perioral Characteristics: The most common oral site for development of these lesions is the maxilla, followed by the mandible. Maxillary involvement manifests as a painless swelling of the affected bone, with possible ulceration of the overlying mucosa. The patient may complain of headache, nasal problems, and separation and/or loosening of the teeth. Figure 18.9A shows a clinical view of a chondrosarcoma with evident bone expansion and mucosal ulceration. Figure 18.9B depicts a radiographic view of a chondrosarcoma showing a radiolucent/opaque destructive process causing widening of the PDL space of an adjacent tooth as well as displacement of adjacent teeth; this is called root divergence. When found in the mandible, they usually involve the premolar and molar regions but may be found in the symphysis and the coronoid and condylar processes. Usually discovered radiographically, the chondrosarcoma may appear as a multilocular or a focal radiolucent lesion, sometimes with opaque features. Widening of the PDL space of affected teeth is another feature commonly seen.

Significant Microscopic Features: Chondrosarcomas are well differentiated with cellular atypia. Multiple cells in the lacunae and cellular pleomorphism are the common features. The chondrosarcomas are graded with the increasing incidence of metastasis. Mitotic figures may be numerous.

Dental Implications: Chondrosarcomas may cause teeth to become mobile. Monitoring the patient periodically for signs of a recurrence is crucial.

Differential Diagnosis: Considerations include:

1. Chondroma: The **chondroma** is a *benign neoplasm* of cartilage tissue that may exhibit features similar to those of the chondrosarcoma. Although rare in the oral cavity, the chondroma affects some of the same sites as the chondrosarcoma but appears even later in life. Histologically, chondromas are masses of hyaline cartilage containing mononuclear chondrocytes. The chondroma is mentioned in the differential diagnosis because

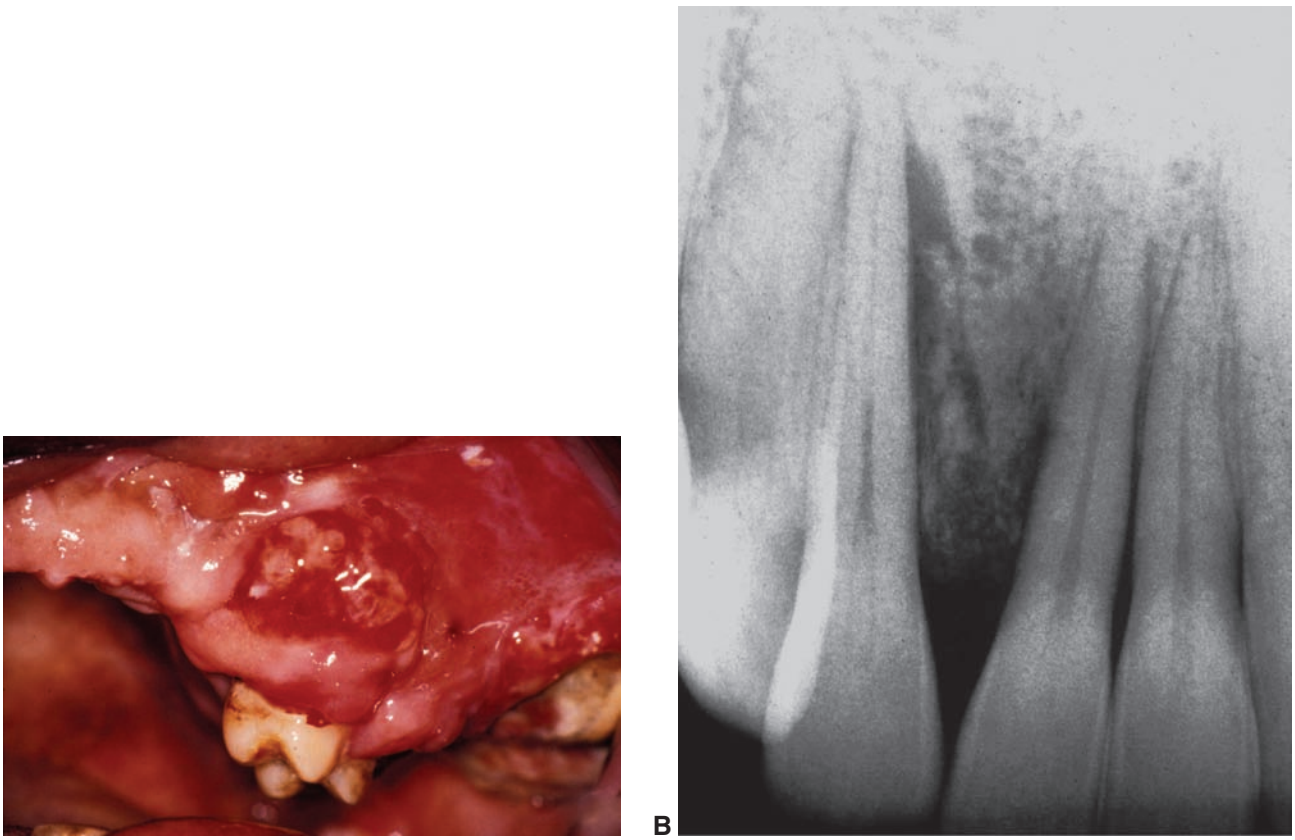


FIGURE 18.9. **A**. Clinical view of a chondrosarcoma. (Courtesy of Dr. Shabnum Meer.) **B**. Radiographic view of a chondrosarcoma. (Courtesy of Dr. Michael Kahn.)

differentiation of chondrosarcoma and chondroma can sometimes be difficult. The chondrosarcoma is similar to the chondroma but cellular atypia is present in the chondrosarcoma specimen.
2. Pleomorphic adenoma, Chapter 17
3. Osteosarcoma, Chapter 18

Treatment and Prognosis: Surgical excision, which can be extensive depending upon the size of the lesion, is the treatment of choice. MRI scans are the most reliable tool in diagnosing the extent of the lesion. These tumors are radioresistant, meaning that radiation therapy is not a treatment option. The 5-year survival rate for patients with high-grade tumors is 15%, but the outlook for patients with low-grade tumors is more favorable. If the tumor recurs, it is usually found 5 to 10 years postsurgery.

NAME: Ewing sarcoma

Etiology: **Ewing sarcoma** is a malignant bone tumor of unknown origin; however, a neural or neuroectodermal origin is suspected. A relationship between the development of this tumor and past irradiation or childhood diseases that required chemotherapy may exist. Radiation-induced Ewing sarcoma is determined by several factors: (1) whether the past radiation occurred at least 5 years prior to the existing state, (2) if the malignancy is in the same area as the past irradiated field, and (3) if the tumor meets criteria of being histologically different from the originally treated disease.

Method of Transmission: Not applicable

Epidemiology: Ewing sarcoma is a malignant bone tumor constituting approximately 4 to 6% of all primary bone tumors and is the second most common malignant bone tumor in children. Approximately 4% of these tumors occur in the head and neck area. This tumor usually affects the under 20-year-old age group, with the sarcoma occurring most often in young children. White males are affected more often than females, but in head and neck cases, there is a nearly equal distribution.

Pathogenesis: This tumor is thought to arise from primitive elements of the bone marrow or mesenchymal cells. Most are also associated with a translocation of genetic material between chromosomes 11 and 22. Both osseous and extraosseous subtypes of Ewing sarcoma exist.

Extraoral Characteristics: During childhood, the lesions of Ewing sarcoma usually involve the long bones such as the femur, tibia, and humerus. When the tumor arises later in life, it affects the pelvic area and the femur more often. A soft tissue in the area of the tumor may be clinically evident.

Perioral and Intraoral Characteristics: When Ewing sarcoma is found in the mouth, the lesions usually involve pain, swelling, numbness, and often tooth mobility. One may also encounter a soft tissue mass in the affected area. The ramus of the mandible is the most common intraoral location for this tumor. Often there is destruction of the alveolar bone and ulceration of the overlying gingiva. The growing tumor may cause facial asymmetry. The lesion appears radiographically as a "moth-eaten radiolucency" or as an infection in the bone, with destruction or erosion of the cortical bone. Additionally, it may exhibit an "onionskin" appearance.

Distinguishing Characteristics: The most distinguishing feature of Ewing sarcoma is the enlarging mass or swelling that is usually present.

Significant Microscopic Features: A sheet-like proliferation of small round cells resembling very large mature lymphocytes is common. The cells are dark staining, with a rim of cytoplasm, and appear vacuolated.

Dental Implications: Any hard tissue growth should be evaluated and diagnosed through biopsy and additional warranted tests.

Differential Diagnosis: Considerations in a differential diagnosis include:

1. Chondrosarcoma, Chapter 18
2. Metastatic cancer. All chapters cover this aspect since this is a risk with most malignancies.
3. Leukemia, Chapter 9
4. Lymphoma, Chapter 9

Treatment and Prognosis: Surgery, radiation, and chemotherapy are the standard treatment. A survival rate of 60 to 80% has been reported in cases of Ewing sarcoma; however, the survival rate has continued to improve. Approximately 20% of those affected will experience metastasis, commonly involving the lungs.

SUMMARY

- The hard tissue enlargements covered in this chapter can be benign or very serious tissue enlargements that are life threatening.
- As with any disease state, early diagnosis is the key to successful treatment and recovery.
- Sometimes subtle changes that the patient may notice such as pressure, loose teeth, or pain may be the first sign of a bone tumor.
- Some lesions are clinically evident; others may be seen initially on radiographs.
- Careful review of the medical history and radiographs along with a thorough clinical examination are all keys in the evaluation of a patient's health.
- Torus palatinus and mandibular tori are composed of normal compact bone and pose no problems in most situations.
- Exostoses are asymptomatic, exuberant, compact bone growths that occur along the maxilla and the mandible.

The growths can be single or multiple nodules composed of dense, compact bone.

- Chronic osteomyelitis with proliferative periostitis is described as a proliferative inflammatory response of periosteum to infection, caused by other irritants.
- Odontogenic tumors arise from epithelial tissue or from mesenchymal remnants of tooth-forming tissues.
- The ameloblastoma is classified as an odontogenic tumor.
- The CEOT has an odontogenic origin. The CEOT is found more often in the mandible, and there is no gender predilection.
- CEOT has distinct concentric calcified deposits known as Liesegang rings.
- The ossifying fibroma, or cementoossifying fibroma, is a benign neoplasm, composed of cementum-like calcifications and bony components.
- The CGCG can grow outside of bone and penetrate through into the soft tissue.
- The osteosarcoma is the most common primary malignant tumor found in bone and accounts for 20% of all bone tumors. In some cases of osteosarcoma, the radiographic appearance may be described as a "sunburst" pattern or a "spiking resorption."
- Chondrosarcoma is a malignant tumor of cartilage.
- Ewing sarcoma is a malignant bone tumor of unknown origin.

CHAPTER REVIEW

Case Study 18.1

A new patient, Kasa Lovelace, a Native American female, age 45, presents for her first full mouth radiographic survey. You have everything set up, including plastic positioning devices and bitewing tabs. You ask Kasa to remove any removable appliances if she has them. As you inspect the mouth before beginning the radiographic series, you palpate the hard palate and discover that the surface is not the normal palate (Fig. 18.10). Your first thought is to wonder how to place a radiographic device in Kasa's palate.

Answer the following questions:

1. What is your best estimate as to the identity of this lesion?
2. What questions would you want to ask Kasa?
3. Would you expect the tissue to be completely firm in all areas?
4. What factors may have contributed to the development of this growth?
5. Would Kasa experience any complications related to this growth other than the problem with positioning radiographic films? Should she have this removed?
6. What are your options for completing your radiographic procedure at this point?

FIGURE 18.10. Clinical view of the palate. (Courtesy of Dr. Alan B. Coleman, DDS, FAGD.)

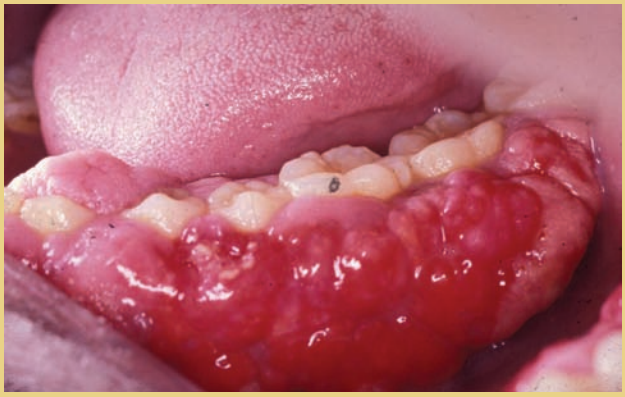
For answers and additional review activities, log in to **thePoint.lww.com**

Case Study 18.2

The 33-year-old male patient depicted in Figure 18.11 has a large area of swelling on the left side of the face and has the following complaints:

- Pain
- Tingling and numbness at times.
- He tells you that he has some loose teeth.
- Presently, he is very feverish and, when you take his body temperature, it is 102°F.
- He tells you that the swelling was noticeably evident 5 months ago and is rapidly increasing in size.

A



B

C

FIGURE 18.11. (All three images courtesy of Dr. Shabnum Meer.)

As you begin to examine the patient's mouth, you notice the gingiva is bulbous on the left side with very firm/hard exostosis. The bone-like material encompasses the molar and premolar area. The external surface is very edematous (Fig. 18.11B).

1. Do you believe that this clinical presentation is a benign lesion or a malignancy?
2. What types of disease states would you consider?

Given what is seen in the radiograph (Fig. 18.11C):

3. What facts about the swelling would you be able to determine?
4. What radiographic findings give you some clues to a diagnosis?
5. How would you determine the diagnosis for this patient? What tests would be needed?
6. Describe how the clinical appearance and signs and symptoms of this lesion would support each of the following types of conditions:
   - Infections
   - Soft tissue tumor
   - Hard tissue tumor
   - **A.** Which of the above conditions do you feel is the most likely?
   - **B.** What recommendations and referrals are appropriate for this patient?

Critical Thinking Activity

1. Early osteosarcoma can present with radiographic evidence and widening of the PDL space.
   - **A.** How do you know if the widened PDL space that you see on one of your patient's radiographs is NOT an osteosarcoma?
   - **B.** What additional information would help to rule out an osteosarcoma?
   - **C.** Should you refer everyone with widened PDL spaces for a biopsy?
   - **D.** What other conditions can present with a widened PDL space?

Portfolio Possibilities

1. Gather some information for patient education on one of the sarcomas including its development, treatment, and prognosis.
2. Consider the fact that until a clinician discovers the torus, the patient may not even be aware of its existence. Once pointed out, the patient may wonder why it is there and if it is a type of pathology. The patient may even touch the area constantly with the tongue and actually irritate the torus. Research tori and collect color slides with various types of torus palatinus, mandibular tori, and exostosis. Write an explanation of the process that could be presented to the patient when a torus or tori are diagnosed.
3. Many of the diseases discussed in this chapter are diagnosed through radiographs. If your office does not have a written policy on the use of radiographs, the rationale for taking them, and stated intervals, this could be an excellent project to develop as a team. Perhaps the written guidelines could be given to new patients with your own stated philosophy regarding their importance in the dental office.

Media Menu

Web Sites

Drug Watch
http://www.drugwatch.com

National Institutes of Health
http://health.nih.gov/

National Library of Medicine MedlinePlus: Oral Cancer
http://www.nlm.nih.gov/medlineplus/oralcancer.html

World Health Organization
http://www.who.int/en/

Study Tools

Take advantage of additional online resources to help you study and ace your exams!

- Answers to case studies in the book
- Additional case studies and answers
- Interactive quiz bank with answer feedback
- Fully searchable e-book for quick lookup and studying on-the-go
- Expanded Media Menu with direct links to related Web sites and multimedia resources
- Supplemental references

thePoint Online resources and links are available at http://thepoint.lww.com/DeLong2e

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Chapter 18 **LESION/CONDITION SUMMARY TABLE**

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Torus Palatinus, Mandibular Torus (torus mandibularis)	Genetic and ethnic predisposition. Masticatory stresses from bruxing and clenching. Environmental, burns, trauma, etc.	Composed of normal compact bone that has reacted to stimulus	Torus palatinus is found in the midline of the palate as an enlarged growth of bone. Mandibular torus is found on the lingual aspect of the mandible and these are usually bilateral (mandibular tori).	Mature, dense, lamellar cortical bone.	The tori are only a problem if a partial or full denture needs to be made. Sometimes they are removed for this reason. Surgical procedures may have complications such as perforation of sinus, bone necrosis, fracture of palatine bone. These should only be performed when absolutely needed.	Occasionally, bony growths may interfere with speech, eating, and toothbrushing.
Exostosis (pl. Exostoses)	Exuberant growth of compact bone	Stressors such as bridges and bruxism	These occur on the facial aspect of the maxillary and mandibular surfaces.	Mature hyperplastic cortical and trabecular bone.	No treatment is recommended.	Night guards may be needed if it is determined that bruxism is the cause. Other disease states must be ruled out such as osteosarcoma, chondrosarcoma and Ewing's sarcoma.
Chronic Osteomyelitis with Proliferative Periostitis (Garré Osteomyelitis)	Inflammatory response of the periosteum to infection or other irritants	An infection, usually of odontogenic origin passes through the cortex of bone and involves the periosteum. The periosteum becomes stimulated and lays down more bone. The layering is called the onionskin pattern.	Appears as a bony hard, asymptomatic protuberance with normal tissue covering the growth. Usually found in the posterior regions of the mandible.	Surface covered by stratified squamous epithelium. Marked thickening of the basal layer and epithelium. Koilocytes are noted. These occur due to extensive replication of the virus.	Removal with scalpel, laser, cryosurgery, or electrosurgery	Diagnosis and treatment will help prevent transmission. Carefully evaluating the etiology of the lesions is needed since medical referral may be needed. If HPV 16 is detected, there is a higher risk of anogenital carcinoma and oropharyngeal carcinoma.
Ameloblastoma: Multicystic, Unicystic or Peripheral (Exostosis)	Most common odontogenic tumor. Usually found in mandible in 20–50 age group.	Arise from epithelial or mesenchymal remnants of the enamel organ, rest of Malassez, rests of Serres, or reduced-enamel epithelium.	Facial asymmetry may be present. Painless swelling usually in the posterior mandible.	Palisading columnar cells around epithelial nests resembling the enamel organ. Elements of the stellate reticulum are present. Peripheral cells resemble ameloblasts with reverse polarity. Ameloblastomas are not encapsulated.	Surgical removal with clear margins. Follow up with periodic radiographs is needed.	Recurrence may be a problem if complete removal is not accomplished.
Calcifying Epithelial Odontogenic Tumor (CEOT) (Pindborg Tumor)	Unknown, but probably due to remnants of the enamel organ.	Locally invasive tumor. Occurs less frequently than the ameloblastoma.	Slow growing painless expansion. Occurs most often in the mandible and in posterior region.	Liesegang rings may be seen microscopically. These are calcified deposits forming within the tumor islands of the specimen. Radiographs may be radiolucent or they may contain obvious calcified material.	Surgical removal of the tumor. Wide margins are needed to prevent recurrence.	The tumors are found during routine exams or when the patient notices swelling. The patient should be followed closely with radiographs.
Ossifying Fibroma (Cementoossifying Fibroma)	Unknown but composed of cementum-like calcification and bony components.	Slow growing, painless and expansile.	Nonpainful swelling. Often undetected clinically but evident in a radiograph. Root resorption or divergence may be seen in radiograph.	Vascular, cellular, fibrous connective tissue with bone fragments. Collagen fibers are arranged in a "storiform pattern" with immature bone and osteoblasts.	Surgical removal.	Prognosis is excellent. These are not malignant and recurrence is rare.

Chapter 18 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Central Giant Cell Granuloma (CGCG)	Believed to be a reactive lesion to trauma or local factors.	The lesions are aggressive and also may recur after removal. Classified as a neoplasm.	Most occur in mandible and maxilla, but can occur on the small long bones of the hands, feet, and face. Usually found on radiograph as a unilocular lesion.	Spindle-shaped mesenchymal cells with focal aggregates of small-multinucleated giant cells. The stroma is that of fibroblasts and fibrosis.	Excision by curettage is recommended treatment.	A recurrence rate of 15–20% is commonly found. Careful monitoring is needed.
Osteosarcoma (Osteogenic Sarcoma)	Occupational exposure to toxic materials, mutation of *Rb* gene and *p3*, past radiation and chemotherapy exposure.	May be found in maxilla and mandible. Long bones may be affected. Males affected more often.	Pain and swelling, loose teeth, numbness. Dysesthesia, burning mouth and tingling.	Classic "sunburst" pattern on radiograph. Spiking resorption. Pleomorphic malignant spindle cells, tumor giant cells and mitosis. Malignant cells producing osteoid.	Chemotherapy with complete removal of bone lesions. Clear margins must be obtained	Tooth mobility, welling and pain are common. Fractures may be a concern. Widening of the periodontal ligament (PDL) is common. This may be a very early sign and should be taken very seriously in viewing radiographs.
Chondrosarcoma	Previous radiation treatment. Environmental exposure and genetic predisposition.	Malignant tumor of the cartilage. May progress to lungs or bones when left untreated. Most common oral site is the maxilla followed by the mandible.	Nasal obstruction, mobility, widening of the PDL. Early development produces no pain. Pain occurs when size increases. Root divergence is often seen.	Cellular atypia, multiple cells in the lacunae and cellular pleomorphism. Mitotic figures may be numerous.	Excision depending upon the size. MRI scans to determine the size.	Follow up and careful monitoring is needed. Any PDL space that is widened should be carefully evaluated. A 5-year survival rate of 15%. May occur in other areas of the body.
Ewing Sarcoma	Unknown origin, but neural or neuroectodermal origin is suspected. Past childhood treatment with radiation and chemotherapy may be the cause of progression.	Tumor thought to arise from primitive elements of the bone marrow or mesenchymal cells. Both osseous and extraosseous subtypes exist.	Lesions involve pain, swelling, numbness, and mobility. Destruction of the alveolar bone, and ulceration of the gingiva.	Radiographically, the lesion appears moth-eaten or as an infection of the bone. Sheet-like proliferation of small round cells resembling very large mature lymphocytes. The cells are dark staining with a rim of cytoplasm and appear vacuolated.	Surgery, radiation, and chemotherapy. There is a 60–80% survival rate. 20% will also have metastasis to lungs.	Any hard tissue growth should be evaluated and a clear diagnosis made. With all detectable and diagnosed entities, close follow up is needed.

CHAPTER 19

Radiopaque Lesions

KEY TERMS

Albers-Schönberg disease (marble bone disease)
Ankylosis
Cementoblastoma
Endosteal
Focal sclerosing osteomyelitis (condensing osteitis)
Gardner syndrome
Hamartomas
Metastatic calcifications
Odontoma
Osteoma
Osteopetrosis
Periosteal
Phleboliths
Polyposis
Tonsilloliths

LEARNING OUTCOMES

1. Define and use the key terms discussed in this chapter.
2. State the most common location for focal sclerosing osteomyelitis.
3. List the various interventions that are indicated in the treatment of focal sclerosing osteomyelitis.
4. Discuss the etiology of diffuse sclerosing osteomyelitis and state the primary cause of the bone lesions.
5. List the significance of discovering an osteoma in a clinic patient.
6. Differentiate between the compound and the complex odontoma.
7. Describe the clinical significance of the cementoblastoma and its effect on the tooth structure.
8. Name and define two types of osteomas.
9. State the origin of osteopetrosis, along with two dental conditions that are associated with the disease.
10. Describe Gardner syndrome and state the importance of its early detection to the patient and the relatives of the patient.
11. List the possible calcifications that may be seen on a Panorex within the submandibular and neck region and discuss the importance of these findings.

CHAPTER OUTLINE

Traumatic or Inflammatory Lesions
- Focal sclerosing osteomyelitis
- Osteomyelitis with Diffuse Lesions

Neoplasms
- Cementoblastoma
- Odontoma
- Osteoma
- Gardner Syndrome

Congenital or Genetic Disorders
- Osteopetrosis

Other Radiopaque Entities

RELATED CLINICAL PROTOCOLS

#11 Patient Education: Oral Cancer Self-Examination
#14 Postoperative Instructions for Oral Surgery Patients
#19 Oral Health Care Management of the Patient with Cancer
#25 How to Utilize Nutritional Counseling in Practice
#26 Helping Relationships for Dental Hygienists
#27 Motivational Interviewing for Behavioral Change

As discussed in Chapter 18, some lesions not only appear clinically, but may also be seen on a radiograph. Other lesions may only be obvious on a radiograph, without exhibiting a clinical appearance. The conditions discussed in this chapter may be seen on a radiograph in various stages of development and are classified as radiopaque lesions. Some of these lesions may be completely opaque, while others may have radiopaque qualities, with varying amounts of radiolucent qualities as well, depending on the stage of development.

Traumatic or Inflammatory Lesions

This section contains a discussion of focal sclerosing osteomyelitis that occurs because of a reaction to a low-grade inflammatory stimulus. The stimulus may be due to pulpitis, or an inflammatory process that causes a reaction in the bone. Also discussed in this section is osteomyelitis with diffuse lesions that may be caused by a microorganism of low virulence. The microorganism gains entry through the caries process, periodontal disease, or through some other port of entry into the tissues.

NAME: Focal sclerosing osteomyelitis (condensing osteitis)

Etiology: **Focal sclerosing osteomyelitis** is an inflammatory reaction that usually involves pulpal inflammation and necrosis. However, it can be associated with a normal tooth as well.

Method of Transmission: Not applicable

Epidemiology: The mandibular molar teeth are usually the prime regions involved, and the first molar is most affected.

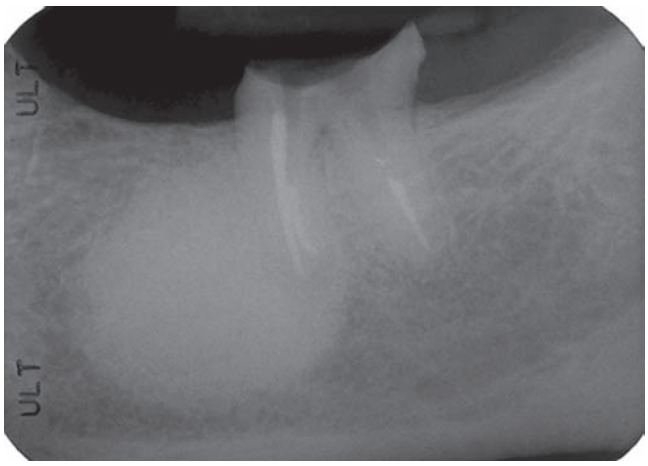


FIGURE 19.1. Focal sclerosing osteomyelitis (condensing osteitis). (Courtesy of Dr. Harvey Kessler.)

Younger age groups are most often reported with focal sclerosing osteomyelitis, and the individuals tend to be under 20 years of age. There is no gender difference with focal sclerosing osteomyelitis as the condition is due to necrosis.

Pathogenesis: Focal sclerosing osteomyelitis is sometimes referred to as *sclerotic bone* or *bony scar*. Local inflammation from pulpitis or pulpal necrosis is often termed "condensing osteitis." The lesion is usually a reaction to some type of trauma or an inflammatory reaction to some stimulus, such as long-standing pulpal involvement. The term "focal" indicates that the lesion is usually isolated to one area, normally involving the apex of the tooth. Figure 19.1 depicts focal sclerosing osteomyelitis (condensing osteomyelitis) in the apical area of the molar.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: The lesions are usually noticed during examination of the radiographs, and the patient may be asymptomatic. The radiograph sometimes exhibits a varying radiopaque area at the apex of the tooth and the surrounding area.

Distinguishing Characteristics: Sclerotic bone without inflammation is usually characteristic; however, depending upon the extent of the lesions, inflammatory lesions may appear with different degrees of lucency. These lesions produce a combination of dense bone and radiolucent patches that may be diffuse and do not exhibit a completely focal opaque appearance.

Significant Microscopic Features: The histologic features of focal sclerosing osteomyelitis include sclerotic trabeculae and fibrous marrow with few lymphocytes.

Dental Implications: The tooth must be treated, and the caries removed. Endodontic treatment may be rendered, depending upon the damage to the tooth.

Differential Diagnosis: Other disease states that may be considered are:

1. Periapical cementoosseous dysplasia, Chapter 20
2. Cementoblastoma, Chapter 19
3. Osteoma, Chapter 19
4. Complex odontoma, Chapter 19

Treatment and Prognosis: The tooth involved is treated by endodontics, extraction, or restoration. In some cases, there may be no treatment rendered, and this is determined on an individual basis. The prognosis of the tooth depends upon the involvement of necrosis or infection, but the osteomyelitis may resolve once the stimulus is removed. Osteomyelitis may be a continuing problem manifesting for varying lengths of time or the sclerotic bone alone may be present indefinitely.

Osteomyelitis with Diffuse Lesions

Infections that appear radiopaque may have varying amounts of density and can extend throughout each quadrant of the mouth. Any osteomyelitis can be focal or diffuse, depending upon the extent of the bony involvement. If large areas of bone are involved, it is technically diffuse. Any osteomyelitis may be sclerosing (producing opaque areas), but many are not sclerosing and appear mostly as radiolucent. True osteomyelitis, whether focal, diffuse, sclerosing, or nonsclerosing, is normally caused by infection. Osteomyelitis that appears diffuse occurs mostly in the mandible, particularly the angle of the mandible, and can extend throughout the affected quadrant. This infection is caused by microorganisms that result in an inflammatory reaction process. Osteomyelitis can arise from periodontal disease, which allows bacteria to enter into the bone region. We have discussed focal sclerosing osteomyelitis in which there is pulpal involvement in an isolated area due to a known stimulus that produces a physiologic bone reaction. Chronic osteomyelitis may include a wider area; the bacteria may be more infectious, and it sometimes involves a long-term, low-grade inflammatory reaction. Figure 19.2 shows osteomyelitis with diffuse lesions exhibiting both opaque and radiolucent areas in the right and left mandibular regions. Diffuse osteomyelitis may occur in a large isolated site or there can be extensive coverage in an entire quadrant as depicted in Figure 19.2.

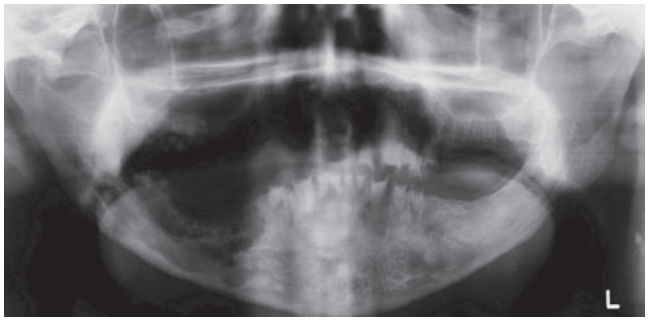


FIGURE 19.2. Diffuse osteomyelitis. (Courtesy of Dr. Enrique Plantin.)

Neoplasms

Neoplasms related to radiopaque lesions, including the cementoblastoma, the odontoma, and the osteomas, are discussed in this section. The radiopaque nature of these lesions makes diagnosis clinically challenging. As previously discussed, diffuse sclerosing osteomyelitis can exhibit both a radiopaque and a radiolucent appearance, depending upon the extent of the lesions and the stage of development. Likewise, some neoplasms may have a varied appearance depending upon their stage of development.

NAME: Cementoblastoma

Etiology: **Cementoblastoma**, also called true cementoma, or true tumor of cementum, is a benign odontogenic tumor. The tumor is characterized by proliferating cementum-like tissue.

Method of Transmission: Not applicable

Epidemiology: Cementoblastomas are usually found in young adults less than 21 years of age. Reports of children much younger (age 8) have been reported (Harada, 2011; Bilodeau, 2010), although the occurrence is rare. There is no gender predilection, although some reports indicate a slight male predilection. The tumors account for 0.08 to 2.6% of all odontogenic tumors (Ohki et al., 2004). The posterior mandible is the most common site of occurrence, but the maxilla is more common when multiple teeth are involved.

Pathogenesis: Cementoblastoma is a true neoplasm of cementoblasts. The lesions may produce pain, and the tooth remains vital. They may be painful or completely asymptomatic until the growth becomes large enough to impinge on other tissues. The cementoblastoma is attached to the tooth root and appears radiographically as an opaque calcified mass. Figure 19.3A depicts a mass of calcification at the apices of a molar.

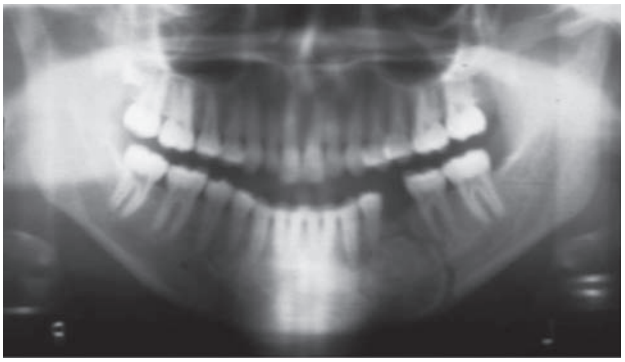
Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: There may be normal pulp tissue that is vital, but because of the disruption of normal neural impulse transmission, the tooth will not test vital with an electric pulp tester. Figure 19.3B shows a cementoblastoma in the mandibular right region and depicts the radiolucent area around the calcification.

Distinguishing Characteristics: When viewed radiographically, the calcified mass has a radiolucent halo around the outer perimeter, which is the periodontal ligament space. Since the calcified mass engulfs the root of the tooth (referred to as **ankylosis**), it is visible on the radiograph. The patient may be with or without pain, and there is usually swelling.

Significant Microscopic Features: The cementoblastoma exhibits dense mineralized cementum with many reversal lines, irregular lacunae, and cellular fibrovascular stromata. Figure 19.3C depicts the histology of the cementoblastoma with the attachment of the tumor at the apical area of the tooth.

A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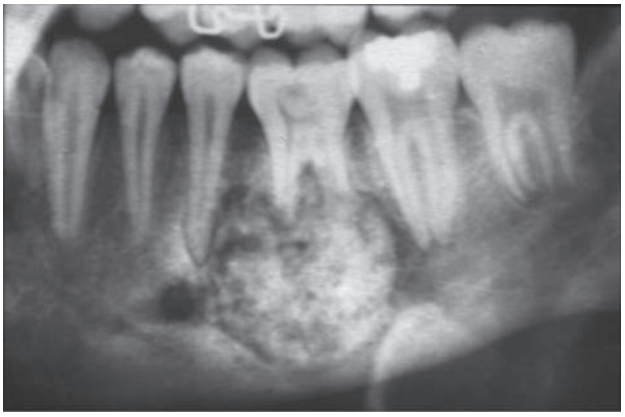
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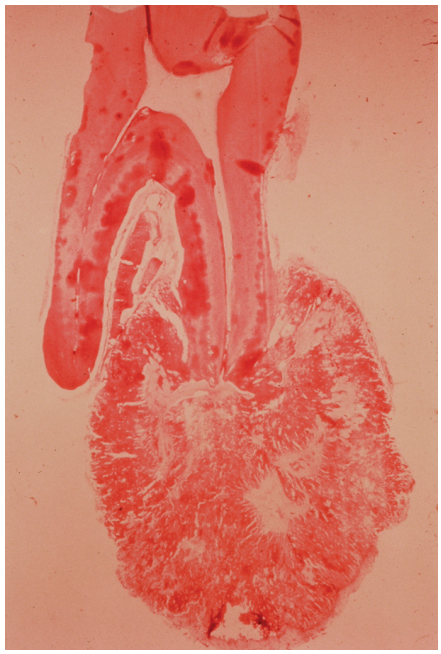

C

E

FIGURE 19.3. **A** and **B**. Cementoblastoma. (Courtesy of Dr. Shabnum Meer.) **C**. Histology of a cementoblastoma. (Courtesy of Dr. John Jacoway.) **D** and **E**. Cementoblastoma. (Courtesy of Dr. Shabnum Meer.)

Dental Implications: The patient may present to the dental practitioner with only symptoms of pain. Therefore, the clinician will be required to categorize the characteristics of the lesion involved, including the stage of development, the vitality of the tooth, and the factors that would indicate that the lesion is a cementoblastoma. Figure 19.3D depicts a large cementoblastoma of the mandibular molar region. Figure 19.3E represents a large cementoblastoma of the mandible, extending from the molar region forward.

Differential Diagnosis: Considerations may include some of the other radiopaque lesions such as

1. Focal sclerosing osteomyelitis, Chapter 19
2. Hypercementosis, Chapter 21
3. Osteoblastoma, Chapter 19
4. Odontoma, Chapter 19

Treatment and Prognosis: The usual protocol is removal of the tooth because of the unlimited growth potential related to the attached calcified mass. This growth potential makes removal necessary even though the tooth tests vital. The prognosis is excellent, without usual recurrence as long as the mass is totally removed.

NAME: Odontoma

Etiology: **Odontomas** are mixed odontogenic tumors comprised of both epithelial and mesenchymal tissues. They are the most commonly occurring odontogenic tumor. Odontomas are developmental anomalies and are **hamartomas** (composed of an abnormal mixture of tissue elements). In the case of odontomas, the tissue involved is a mixture of enamel, dentin, cementum, and pulp. They are believed to be a disturbance in tooth development triggered by infection or trauma. There is also a hereditary component.

Method of Transmission: Not applicable

Epidemiology: The age group most commonly affected is individuals under age 20, and there is no sex predilection (Buchner et al., 2006). Studies to determine the relative frequency of central odontogenic tumors in relation to all biopsy specimens submitted to a biopsy service reviewed 91,178 dental cases. Of that number, 1,088 biopsy results were central odontogenic tumors. The odontoma was the most common type (75.9%), with the ameloblastoma the second most commonly found (Buchner et al., 2006).

Pathogenesis: The odontoma is a mixture of both epithelial and mesenchymal dental hard tissues. Two forms of the odontoma exist:

1. **Compound odontoma** resembles small teeth and appears in a collection of calcified material. Figure 19.4A depicts a clinical view of the compound odontoma with tooth-like structures at the surface of the gingival tissue of an adult.
2. **Complex odontoma** consists of a collection of hard tissue and includes deposits of enamel, dentin, cementum, and pulp all together in a mass-like calcified form. Figure 19.4B shows a complex odontoma with a mass of calcified structures of the odontoma. In a radiographic evaluation, the complex odontoma is an opaque structure that is not distinguishable as a "tooth" structure.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: The complex odontoma is usually found in the posterior mandibular region, while the compound odontoma is most often seen in the anterior maxilla. The compound odontoma may be evident when normal eruption patterns do not occur and may block the permanent tooth from erupting. This is especially noticeable when the failure to erupt is unilateral. Figure 19.4C depicts an unerupted permanent tooth blocked by a compound odontoma.

The odontomas are usually asymptomatic and discovered on routine radiographs. The complex odontoma usually appears on a radiograph as a calcified mass and sometimes may exhibit some radiolucent properties, depending upon the stage of development.

Distinguishing Characteristics: The complex odontoma and the compound odontoma may be found on a radiograph during a dental examination. However, further histology tests are needed to differentiate the complex odontoma from the compound odontoma. Complex odontomas appear radiographically more amorphous (without definite form or shape) and as solitary forms of indistinct radiopacities, rather than tooth-like structures (Oner & Pocan, 2006). Figure 19.4D depicts a compound odontoma that shows small tooth-like structures. This is a compound odontoma. This is in contrast to the complex odontoma in Figure 19.4B. Figure 19.4B depicts a mass-like structure having no radiographic qualities of tooth-like structures. The confusion can occur in the differentiation of the two types and histologic examination is needed for a definitive diagnosis. Some odontomas may show features of both the complex and compound variety.

Significant Microscopic Features: The elements of enamel, dentin, cementum, and pulp are present in the odontoma. The separate structures may be observed in a tissue sample and viewed under the microscope.

Dental Implications: The odontoma may be seen in Gardner syndrome (discussed in the next section) along with the osteoma. The odontoma may impinge on teeth, causing a failure to erupt, and may also grow in size, causing facial asymmetry.

Differential Diagnosis: Other entities that should be considered are:

1. Osteoma, Chapter 19
2. Cementoblastoma, Chapter 19
3. Periapical cementoosseous dysplasia, Chapter 20

Treatment and Prognosis: Excision is the treatment of choice; the prognosis is excellent without incidence of recurrence.

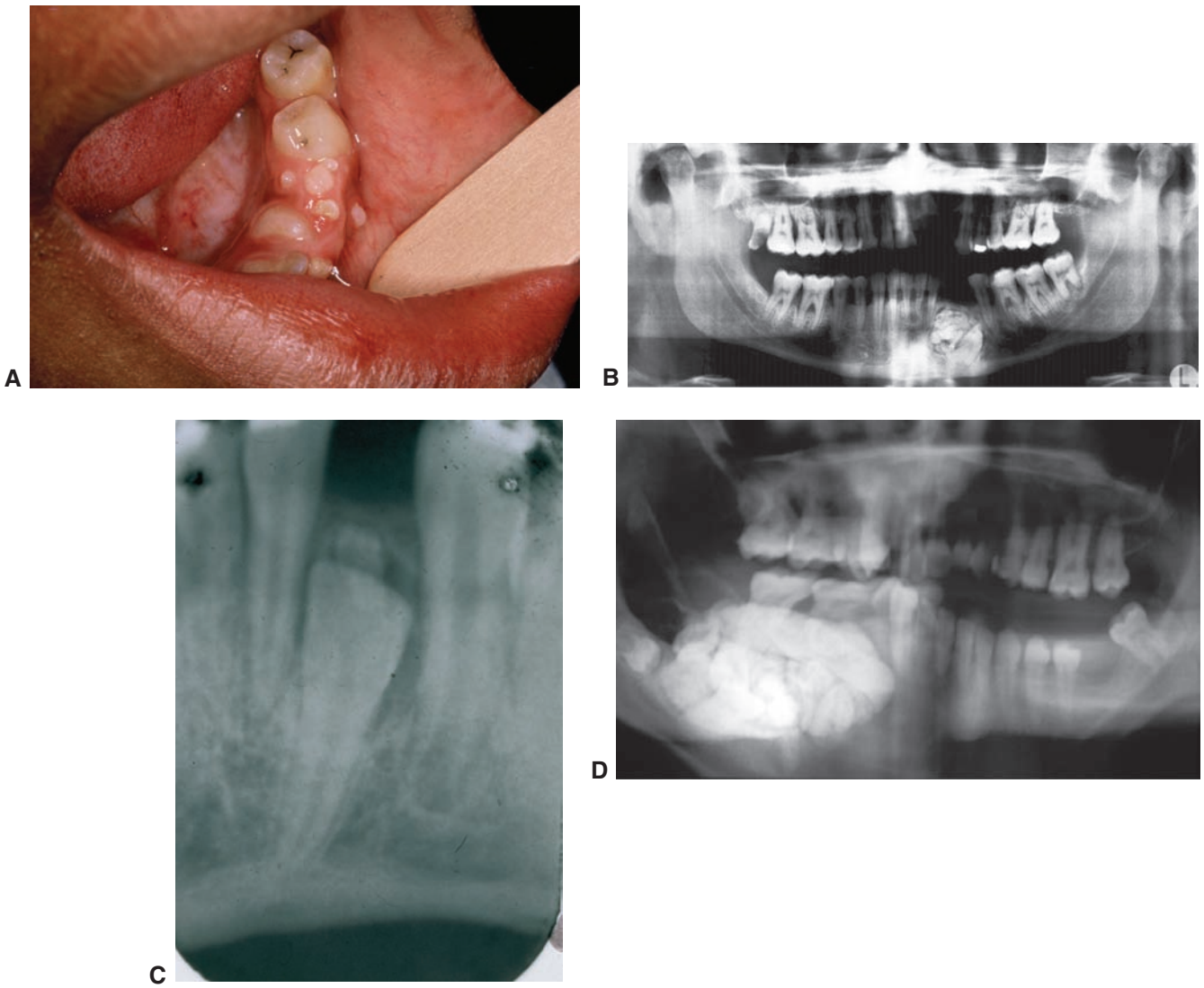


FIGURE 19.4. **A**. Compound odontoma. (Courtesy of Dr. John Jacoway.) **B**. Complex odontoma. (Courtesy of Dr. Enrique Platin.) **C**. Compound odontoma preventing eruption. (Courtesy of Dr. John Jacoway.) **D**. Compound odontoma. Note the small tooth-like structure to the left of the mass. (Courtesy of Dr. A. Yusuf Oner.)

NAME: Osteoma

Etiology: The origin of the osteoma is unknown, but trauma, infections, and developmental defects have been suggested as possible causes.

Method of Transmission: Not applicable

Epidemiology: Osteomas occur in the second to fifth decade of life, and males are affected more often than females. The growths may occur in the maxilla and mandible, the skull, and the sinuses (Bilkay et al., 2004).

Pathogenesis: The **osteoma** is a benign tumor consisting of mature compact or cancellous bone. Osteomas may be classified as either **periosteal**, occurring on the surfaces of bone, or **endosteal**, occurring in the bone. Although rare, the osteoma may also occur in other facial bones, such as the sinus areas. The osteoma is slow growing, but may eventually reach larger sizes, causing expansion and deformity. The patient sometimes notes facial asymmetry. Osteomas are considered hamartomas along with the odontoma, and both may occur in relation to Gardner syndrome. Multiple osteomas are the hallmark of Gardner syndrome (discussed in the next section).

Extraoral Characteristics: Depending upon the size of the osteoma, some swelling may be noticed extraorally, which may be subtle since the lesion is slow growing. The patient may report noticing this for years before the actual diagnosis.

Perioral and Intraoral Characteristics: Osteomas appear radiographically as a dense opaque growth on the bone. The bony growths may be in the condyle, mandible, and maxilla, or even in the sinus region. Depending upon the size, the patient may be asymptomatic or may experience headaches, sinusitis, or vague related symptoms. Osteomas may be confused radiographically with odontomas and often must

FIGURE 19.5. Gardner syndrome osteomas. (Courtesy of Dr. Enrique Platin.)

be differentiated histologically by biopsy. Figure 19.5 depicts an osteoma in multiple areas of the maxilla and mandible.

Distinguishing Characteristics: Osteomas usually exhibit certain characteristics, such as a sharply defined radiopaque structure with clumped calcifications that resemble tooth-like structures. A radiolucent rim is sometimes seen on the periphery of the lesion.

Significant Microscopic Features: Osteoclast and osteoblast activity and normal bone pattern are evident. Depending upon the type of osteoma, the bone pattern varies. Compact and cancellous bone osteomas are both possible.

Dental Implications: The dental implications make differentiation of an osteoma especially important in the early diagnosis of Gardner syndrome. The presence of osteomas and odontomas may indicate Gardner syndrome and thus the need for further tests (see Gardner syndrome).

Differential Diagnosis: Osteomas may have characteristics that appear similar to those of the complex odontoma. Supernumerary teeth, osteomas, and odontomas are also common occurrences in Gardner syndrome. Radiographically, an osteoma is sometimes similar to the complex odontoma; however, viewing the tissue under the microscope will differentiate the two.

The following would be considered as possible diagnoses:

1. Exostoses, Chapter 18
2. Cementoblastoma, Chapter 19
3. Odontoma, Chapter 19
4. Focal sclerosing osteomyelitis, Chapter 19

Treatment and Prognosis: Observation is the protocol for very small osteomas, with careful monitoring in some cases and surgery for the larger, more extensive, lesions. The prognosis is excellent when the osteoma is removed, and recurrence is usually not a problem. A biopsy and histologic diagnosis is necessary to differentiate the lesions from other pathology, thus the lesions are usually removed anyway for complete diagnosis. Osteomas remain benign, but they may be associated with other disease states, such as Gardner syndrome. Referral to a medical doctor is necessary when there is an indication of Gardner syndrome. Intestinal resection is often performed when there are intestinal polyps indicating Gardner syndrome.

Gardner Syndrome (Familial Colorectal Polyposis)

Gardner syndrome is inherited as an autosomal dominant disorder characterized by polyposis coli (**polyposis**) associated with multiple hard and soft tissue tumors. The syndrome manifests osteomas of the bones and sometimes odontomas, epidermoid cysts, supernumerary teeth, other benign tumors of the skin and soft tissues, gastrointestinal polyps, and multiple polyps. Figure 19.5 depicts osteomas in a Panorex, exhibiting the sharply defined, clumped radiopaque structures of Gardner syndrome.

If left untreated or unrecognized, the polyps associated with Gardner syndrome usually develop into malignant invasive adenocarcinoma in the gastrointestinal tract and the stomach by the fourth decade or before (Brucoli et al., 2011). Polyposis coli occurs in approximately 1 in 8,000 individuals and is the most common form of the hereditary polyposis syndromes (Oner & Pocan, 2006). Gardner syndrome may produce both osteomas and odontomas in both the mandible and maxilla, although the mandible is the favored location. Facial bones may also be involved and develop osteomas leading to facial asymmetry. When recognizing an osteoma, and especially multiple osteomas, the clinician should be aware that the osteoma is the hallmark of Gardner syndrome. Early treatment of the patient with Gardner syndrome is crucial, since there is a fatal outcome of malignancy in relation to the polyps that accompany the syndrome (Fichter et al., 2011). The polyps have a 100% risk of undergoing malignant transformation (Bilkay et al., 2004). Family members should be advised to have screenings for Gardner syndrome as well, since it is a variant of familial adenomatous polyposis. As a dental professional, the clinician can play a crucial role in the recognition of the disorder in association with the osteomas and odontomas that may be found during a routine dental visit.

Osteomas may produce few or no symptoms, and they may only be discovered during a dental visit, becoming apparent on a routine radiograph. Larger, more significant osteomas may cause problems as they impinge upon surrounding tissues and produce some extraoral facial swelling. Providing treatment at the earliest stage in Gardner syndrome is very important in the prognosis of the disease for both the patient and family members.

Congenital or Genetic Disorders

Congenital or genetic disorders related to radiopaque lesions are sometimes not diagnosed until the clinician takes a radiograph or the patient exhibits some symptom indicating that there may be a problem. Sometimes, in mild cases involving bone disorders, the person may not experience problems until later in life. The disease discussed below, osteopetrosis, is a disease that may go undetected

until the patient has a radiograph made or there is a problem encountered during an extraction.

NAME: Osteopetrosis

Etiology: **Osteopetrosis**, also known as **Albers-Schönberg disease** and **marble bone disease**, is a congenital sclerosing disease of bone characterized by osteoclastic dysfunction. Several types of osteopetrosis are possible in this group of genetic bone disorders: autosomal recessive, intermediate autosomal recessive, and autosomal dominant.

Method of Transmission: Osteopetrosis has a hereditary component that is expressed as an autosomal recessive and autosomal dominant disorder, depending upon the type of osteopetrosis.

Epidemiology: The age of the individual affected will vary with the type of osteopetrosis diagnosed. The autosomal recessive form may be evident in the infant; the intermediate autosomal recessive form may become obvious in the first decade of life. The benign autosomal dominant form may become apparent as increasing bone disturbances occur in midlife. Osteopetrosis occurs equally in males and females. The development of osteopetrosis occurs almost exclusively in the mandible (Barry & Ryan, 2003).

Pathogenesis: Osteopetrosis is a genetic disease with varying degrees of bone involvement. The disorder is characterized by a noted increase in the density of the bone, due to reduced osteoclastic activity, along with defective bone resorption (Ihde et al., 2011). As discussed above, the condition is hereditary and is categorized into several groups. The first type, autosomal recessive form found in infants, has a fatal outcome within several years. A second type, the intermediate autosomal recessive form, is very aggressive. The third type is an autosomal dominant type, which manifests noted bone involvement. Obviously, the second and third types may be found clinically as the disorder progresses. The recessive types are found in approximately 1 per 200,000 (Filho et al., 2004). The benign autosomal dominant type has been documented in approximately 50 cases.

Extraoral Characteristics: Prognathic profiles are often a clinical sign of osteopetrosis. These are shown in Figure 19.6, which illustrates the advanced stage of osteopetrosis with dense, generalized sclerosis of the mandible.

Perioral and Intraoral Characteristics: Radiographically, there is skeletal density due to diffuse sclerosing of all the bones. Clinically, there is delayed tooth eruption, enamel hypoplasia, defects in the periodontal membrane, and thickened lamina dura. Bone fractures and osteomyelitis are also problems for the patient. The infantile form of the disorder often exhibits frontal bossing, snub nose, and facial deformity.

In the adult form, the bone becomes more involved as the patient ages, and multiple bone fractures, anemia, and malformation of dental crown and root canals are evident, with pseudo odontomas often present. Osteomyelitis is another complication, and bone fractures are common as well. Often, osteopetrosis is diagnosed when these types of events occur, and at a time when radiographs are routinely made (Filho et al., 2004).

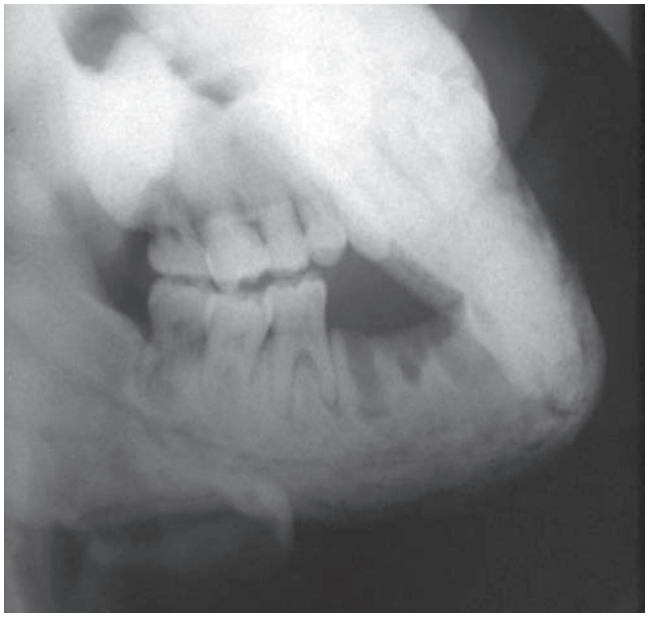


FIGURE 19.6. Osteopetrosis. (Courtesy of Dr. John Wright.)

Distinguishing Characteristics: Radiographs show increased bone density with an amorphous aspect, marrow space encroachment, and malformed teeth that may appear clinically as the odontoma discussed above.

Significant Microscopic Features: Histologically, there is evidence of decrease in osteoclastic function. Additionally, there is a deficiency of bone resorption and bone remodeling, and increased bone density. Diagnosis is made on the history of previous fractures and the radiographic findings of osteosclerosis, along with the histologic results.

Dental Implications: The relevance to the clinician of osteopetrosis is great, because approximately 10% of patients report osteomyelitis in conjunction with osteopetrosis. An existing dental problem may cause the patient to seek treatment, and the osteopetrosis may be diagnosed during routine treatment. Osteomyelitis may be a complication in tooth extraction or trauma, and bone fractures may occur during extractions. Often delayed tooth eruption is a clinical manifestation in children.

Differential Diagnosis:

1. Paget disease, Chapter 10
2. Hyperparathyroidism, Chapter 7
3. Acromegaly, Chapter 7
4. Malignant bone disease, Chapter 18

The main concern related to this disease is a failure to recognize the disorder when treating the patient for extractions. The patient may suffer multiple bone fractures when pressure is applied.

APPLICATION 19.1

Osteopetrosis is a good example of a disorder that is beyond the routine treatment for a dental practice, since treatment involves a multidisciplinary approach. Many individuals are involved in both the diagnosis and the treatment of these patients. Some crucial specialty areas are radiology, pathology, oral surgery, periodontology, prosthodontics, and specialists who treat bone diseases. Additionally, the hygienist, nutritionist, and others who would be involved in both medicine and dentistry for the care of the patient with osteopetrosis, would need to provide adjunctive care.

The best place to find all the specialists together is a medical and dental school or a teaching hospital that accommodates all the various specialists in one area. The patient would be assured of the best possible care with many specialists planning his or her care. The general practitioner and possibly the dental hygienist may be the first professionals to recognize that there is a problem such as osteopetrosis and should refer the patient to the correct facility for initial treatment.

Treatment and Prognosis: It is suggested (Filho et al., 2004) that the patient who is diagnosed with osteopetrosis in any form be seen in a dental school for treatment related to the teeth or oral structures, since a multidisciplinary approach is needed for adequate care (see Application 19.1). Antibiotics are prescribed when needed, as in the case of osteomyelitis with incision and drainage. Hyperbaric oxygen is often recommended as an adjunct treatment in the case of osteomyelitis. Prophylaxis with fluoride is recommended to aid against caries, and restorative dental procedures are part of the protocol. The infantile form has a poor prognosis, with most dying from anemia or infection. The adult form has a better prognosis and may be diagnosed during routine dental examinations as the disease progresses.

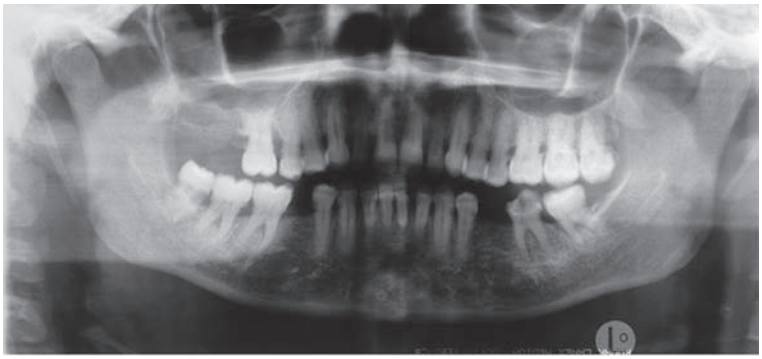
Other Radiopaque Entities

Another entity that should be discussed under radiopaque lesions is the calcification that is sometimes witnessed on a Panorex in the carotid and lymph node locations. These lesions may not have any symptoms and may not even be palpable, but may be clearly visible on the Panorex. The carotid calcification can cause significant vascular occlusion leading to a stroke; therefore, early detection and identification may save the person's life.

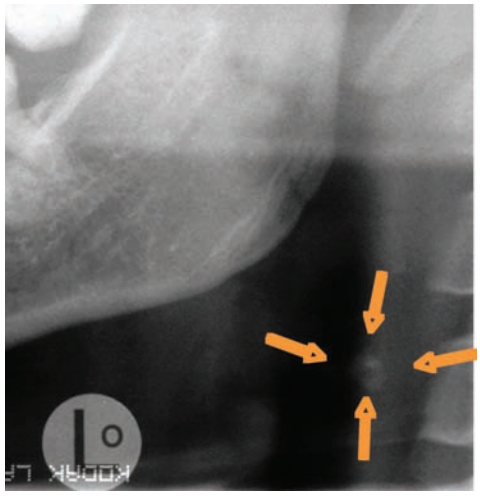
Calcified lymph nodes are typically evidence of past infection rather than metastatic disease, such as carcinoma. In the presence of an elevated serum calcium level, such calcifications may be referred to as **metastatic calcifications**. This term means calcification that is occurring in nonosseous tissue (i.e., nonbone, such as the lymph tissue) and tissue that is not degenerated or necrotic. The cells of these organs secrete acidic materials, and under certain conditions, in instances of hypercalcemia, the alteration in pH causes precipitation of calcium salts in these sites. In the past, the most common cause for calcified nodes was tuberculous lymphadenitis (scrofula). At present, it is more likely due to some other infectious process, with multiple recurrences eventually producing fibrosis within the node that subsequently calcifies. Additional radiographic surveys may be needed to determine that the calcifications are in the lymph nodes and not the carotid artery, which could be a serious medical problem.

Figure 19.7A shows a carotid calcification detected on a routine Panorex. A closer view of this calcification is shown in Figure 19.7B.

Carotid calcifications are rarely reported, but many may be overlooked in the dental office because of their subtle appearance in most cases. Other calcifications appear in a Panorex and may be noted as well, such as



A



B

FIGURE 19.7. **A** and **B**. Carotid artery calcification. (Courtesy of Dr. Enrique Platin.)

calcified lymph nodes, **phleboliths** (a calcified deposit in a venous wall or thrombus), submandibular salivary gland sialoliths, and **tonsilloliths** (concretion in a tonsil crypt) (Pornprasertsuk-Damrongsri & Thanakun, 2005). Normal anatomy and artifact must be differentiated as well and sometimes must be differentiated from normal tissue when the appearance is questionable. Pornprasertsuk-Damrongsri and Thanakun (2005) also found higher rates of hypertension, diabetes mellitus, and hyperlipidemia in patients who were confirmed to have carotid artery calcifications.

SUMMARY

- In many cases, radiopaque lesions are complicated to diagnose because there is often not much clinical evidence manifested during an oral examination. Therefore, a radiograph is necessary to provide the needed diagnostic information related to these disease states.
- The clinician can play a powerful role in detecting obvious changes in dental conditions and, most importantly, those subtle changes that can affect the life of the patient.
- Disorders that have radiopaque lesions as part of other syndromes, such as Gardner syndrome, have profound effects on many areas of the body, making early diagnosis and treatment crucial.
- Gardner syndrome is an inherited autosomal dominant disorder that involves the osteoma and sometimes odontomas, epidermoid cysts, supernumerary teeth, and other benign tumors of the skin and soft tissues, and multiple polyps as part of the disease state.
- The polyposis coli (polyposis) in Gardner syndrome have a 100% risk of undergoing malignant transformation.
- The complex odontomas are usually found in the posterior mandibular region appearing as calcified masses of opaque material, while the compound odontomas are most often seen in the anterior maxilla and exhibit a tooth-like quality.
- The compound odontoma may be evident when normal eruption patterns do not occur and may block the permanent tooth from erupting. Odontomas are mixed odontogenic tumors composed of both epithelial and mesenchymal tissues. Odontomas are developmental anomalies and are hamartomas (composed of abnormal mixtures of tissue elements).
- Osteomas appear radiographically as dense opaque growths on the bone.
- Focal sclerosing osteomyelitis usually involves pulpal inflammation and necrosis of the pulp. Any osteomyelitis may be sclerosing (producing opaque areas), but many are not sclerosing and appear radiolucent or a mixture of opaque and radiolucent.
- Cementoblastoma, also called true cementomas, or a true tumor of cementum, is a benign odontogenic tumor.
- Osteopetrosis is a genetic disease occurring with varying degrees of bone involvement. Osteopetrosis requires a multidisciplinary approach, and the treatment involves many specialists in both medical and dental fields. The failure to recognize the disease prior to extraction may result in facial fractures.

CHAPTER REVIEW

Case Study 19.1

Figure 19.8 is of a 57-year-old male who was seeking routine dental treatment at a clinic. He had no obvious health problems and was taking no medications. He needed a routine prophylaxis and dental examination. During routine radiographs, the clinician noticed that small opaque areas were evident on the Panorex in the posterior mandible and neck area.

1. What would you have considered in viewing this radiograph?
2. What are some possibilities?

FIGURE 19.8. Courtesy of Leslie DeLong, RDH.

For answers and additional review activities, log in to **thePoint.lww.com**

Case Study 19.2

The radiograph presented in Figure 19.9 is that of an odontoma. What features of the radiograph would cause you to classify this entity as a complex or a compound odontoma? State your rationale for the classification (Fig. 19.9).

For answers and additional review activities, log in to **thePoint.lww.com**

FIGURE 19.9. (Courtesy of Ms. Sherri Lukes, RDH, MS.)

Critical Thinking Activity

You have just finished a maintenance appointment with a patient who was recently referred to an oral surgeon for the extraction of #17 and #32. Upon evaluation of the patient's radiograph, the oral surgeon became suspicious of some areas in the radiograph and the patient was referred for additional tests. The patient was ultimately diagnosed with osteopetrosis, also known as Albers-Schönberg disease. Fractures are common, and care with extractions is needed because of the fragility of the bones. The disease causes an increase in bone density and reduction of marrow spaces.

1. Do you think the patient has a defective function of the osteoclasts or the osteoblasts?
2. What is the cause of osteopetrosis?
3. Can you explain the functions of both osteoclasts and osteoblasts?
4. Can you explain how the patient would develop the characteristic prognathic profile?

Portfolio Possibilities

Research the vast array of resources in your area that provide both dental treatment and medical treatment in one facility. The facilities should be able to treat patients who are diagnosed with diseases such as osteopetrosis and Gardner syndrome.

- Make a list of the facilities with each specialty area noted.
- Acquaint yourself with key individuals who would be willing to treat special needs patients upon the referral of your office.
- Design a letter stating that your practice is referring a patient with a suspected disease. A specific form letter is appropriate and could be modified for each patient's needs.
- If there are no facilities close to your practice, find ones that are within a reasonable travel distance for a patient.

Media Menu

Web Sites

National Organization for Rare Diseases: Osteopetrosis
http://www.rarediseases.org/rare-disease-information/rare-diseases/byID/354/viewAbstract

Oral Medicine Association: Oral Cancer Exams
http://www.aaom.com/displaycommon.cfm?an=1&subarticlenbr=95

World Health Organization
http://www.who.int/en/

Study Tools

Take advantage of additional online resources to help you study and ace your exams!

- Answers to case studies in the book
- Additional case studies and answers
- Interactive quiz bank with answer feedback
- Fully searchable e-book for quick lookup and studying on-the-go
- Expanded Media Menu with direct links to related Web sites and multimedia resources
- Supplemental references

thePoint Online resources and links are available at http://thepoint.lww.com/DeLong2e

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Oner AY, Pocan S. Gardner's syndrome: a case report. Br Dent J 2006;24(12):666–667.

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Chapter 19 **LESION/CONDITION SUMMARY TABLE**

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Focal Sclerosing Osteomyelitis (Condensing osteitis, Also known as sclerotic bone, body scar)	Inflammation usually involving the pulp and necrosis. Reaction to a traumatic stimulus.	Reaction to trauma or an inflammatory reaction to a stimulus. Usually located in one area of tissue. Diffuse osteomyelitis may cover a large area of tissue. Usually found in the angle of the mandible.	The lesions may produce a combination of dense bone and radiolucent patches. They may be diffuse or appear as an opaque entity.	Sclerotic trabeculae and fibrous marrow with few lymphocytes.	Endodontics, extraction or restoration of the tooth. Sometimes, no treatment is rendered. The osteomyelitis may resolve once the stimulus is removed.	Caries removal or tooth removal depending upon the damage to the tooth. Endodontic treatment is often needed. Resolution of any infection in the area. Careful monitoring of the existing lesion or future lesions is needed.
Cementoblastoma	Most common site is mandibular molar region in the under-25 age group.	True neoplasm of cementoblasts. Tooth remains vital and pain may be present. The cementoblastoma is attached to the root of a tooth.	Pulp tissue is vital, but will not test vital when an electric pulp tester is used.	Radiolucent halo around the calcified structure. The "halo" is the periodontal ligament (PDL).	Excision of the tooth.	The correct diagnosis is crucial since the patient may complain of pain, but the tooth will not test vital. Good follow up with any abnormality is important.
Odontoma	Mixed odontogenic tumors composed of epithelial and mesenchymal tissues. They are believed to be a disturbance in tooth development.	Compound: resembles small tooth-like structures Complex: a collection of calcified structures all together in a mass	Complex: usually found in the posterior mandibular region Compound: often found in the anterior region and may block tooth eruption.	The structures microscopically have elements of enamel, dentin, cementum and pulp.	Removal of the odontoma.	Gardner syndrome is associated with both odontoma and osteomas. A careful assessment of the patient's health and referral for assessment is advised. See section on Gardner syndrome.
Osteoma	Trauma and infections as well as developmental defects.	Benign tumor consisting of mature compact or cancellous bone. May be periosteal (occurring on surfaces of bone) or endosteal (occurring in the bone).	Usually occur in facial bones or sinuses. Slow growing but reach larger sizes, causing compression and deformity. Considered a hamartoma. Multiple osteomas are a hallmark of Gardner syndrome (see section on topic).	The structure exhibits a radiographic view of a radiolucency around the calcified structure. Osteoclast and osteoblast activity and normal bone pattern are exhibited. Compact and cancellous bone osteomas are both possible.	Surgical removal for large growths. Careful monitoring for smaller growths. These are usually removed anyway so that a diagnosis can be made.	Evaluation for Gardner syndrome is needed. Monitoring is often the treatment for small osteomas and surgery for large ones. They are usually removed completely because a biopsy is needed to have a true diagnosis. Recurrence is not an issue.
Osteopetrosis (Albers-Schönberg disease, marble bone disease)	Autosomal dominant disease of bone. The intermediate type is an autosomal recessive disease.	May occur in young or middle-aged individuals depending upon the type of osteopetrosis. Osteoclastic function is decreased and the bone does not resorb.	Slow growing painless expansion. Occurs most often in the mandible and in the posterior region.	Decreased osteoclastic function. Evidence of a deficiency of bone resorption and bone remodeling with increased bone density.	Facial structures may fracture with extreme pressure when extracting teeth. Eruption failure in children may be a sign of osteopetrosis. Osteomyelitis may occur in conjunction with osteopetrosis.	The tumors are found during routine exams or when the patient notices swelling and/ or when osteomyelitis occurs. The patient should be referred to a dental facility that treats rare disorders and one that has a multidisciplinary component.

CHAPTER 20

Radiolucent Lesions

KEY TERMS

Adenomatoid odontogenic tumor (AOT)
Ameloblastic fibroma
Aneurysmal bone cyst
Bohn nodules
Botryoid odontogenic cyst
Calcifying odontogenic cyst
Caseous necrosis
Cementoma
Cementoosseous dysplasia
Cyst
Dentigerous cyst
Epithelial rests
Eruption cyst
Florid cementooseous dysplasia
Focal cementooseous dysplasia
Glandular odontogenic cyst
Inflammatory Cysts
Langerhans cell disease
Lateral periodontal cyst
Lumen
Nevoid basal cell carcinoma syndrome
Nonvital tooth
Odontogenic cysts
Odontogenic keratocysts
Odontogenic myxoma
Osteomyelitis
Paradental cyst
Periapical cementooseous dysplasia
Periapical granuloma
Precystic epithelial proliferation
Primordial cyst
Pseudocyst
Radicular cyst
Residual cysts
Rests of Malassez
Rests of Serres
Sequestrum
Static bone cyst
Traumatic bone cyst

LEARNING OUTCOMES

1. Define and use the key terms listed in this chapter.
2. Describe how a cyst develops.
3. Describe the origin and identifying characteristics of the radicular cyst.
4. List and describe the three types of cementoosseous dysplasia.
5. State the characteristics of the aneurysmal bone cyst.
6. Compare and contrast the traumatic bone cyst and the aneurysmal bone cyst.
7. Describe the radiographic characteristics of the dentigerous cyst and the odontogenic keratocyst.
8. Discuss the radiographic appearance of the lateral periodontal cyst.
9. List the factors involved in the nevoid basal cell carcinoma syndrome.
10. Note the two forms of the odontogenic keratocyst and explain its relationship with basal cell nevus syndrome.
11. State the histologic finding that is a key diagnostic feature of the calcifying odontogenic cyst.
12. Identify the location of the globulomaxillary cyst.
13. State the importance of a correct diagnosis for the glandular odontogenic cyst.
14. Discuss the origin of the static bone cyst.
15. List and describe the three classifications of Langerhans cell disease.
16. Identify the characteristics of the glandular odontogenic cyst.

CHAPTER OUTLINE

Traumatic or Inflammatory Lesions
- Periapical granuloma
- Radicular cyst
- Aneurysmal bone cyst
- Traumatic bone cyst
- Cementoosseous dysplasia
  - Focal cementoosseous dysplasia
  - Florid cementoosseous dysplasia

Infections
- Osteomyelitis—acute and chronic forms

Developmental Cysts
- Lateral periodontal cyst
  - Gingival Cyst of the Adult
- Dentigerous cyst
- Eruption cyst
  - Gingival Cyst of the Newborn
- Odontogenic keratocyst
  - Nevoid Basal Cell Carcinoma Syndrome
  - Primordial Cyst
- Calcifying odontogenic cyst
- Globulomaxillary cyst
- Glandular odontogenic cyst
- Nasopalatine canal cyst
  - Median Palatine Cyst
- Static bone cyst

Neoplasms
- Adenomatoid odontogenic tumor
- Odontogenic myxoma
- Ameloblastic fibroma
- Langerhans cell disease

RELATED CLINICAL PROTOCOLS

#11 Patient Education: Oral Cancer Self-Examination
#12 Adjunctive Oral Premalignant Screening Devices
#14 Postoperative Instructions for Oral Surgery Patients
#18 Supplements for Oral/Systemic Health
#25 How to Utilize Nutritional Counseling in Practice
#26 Helping Relationships for Dental Hygienists
#27 Motivational Interviewing for Behavior Change

As discussed in Chapter 19, lesions that are radiopaque appear to have a dense white presentation on the radiograph. Oftentimes, lesions may have a combined radiopaque and radiolucent appearance, depending upon the stage of calcification involved. An example is the cementoblastoma (discussed in chapter 19), which manifests a halo effect with the radiolucent lesion appearing as a darker area on the radiograph and forming a definite contrast between the lesion, the bone, and the existing tissue. This chapter discusses the development of these types of cysts and the common cysts that the dental hygienist may view on a radiograph as well as a few that are not often seen, but that certainly need to be identified because of their destructive nature. Radiolucent lesions that are seen clinically, such as bone cysts, cementoosseous dysplasia (COD), and certain neoplasms are also discussed.

Odontogenic cysts are cysts with an epithelial lining composed of the remnants of the tooth-forming organ, such as the rests of Malassez or epithelial rests in the periodontal ligament, glands of Serres (rests of the dental lamina), and reduced enamel epithelium (remnants of the enamel organ). Odontogenic cysts, including the radicular cysts, are presented in the next section. Some cysts that are addressed in this chapter do not have an epithelial lining and are not true cysts, but are termed pseudocysts.

Traumatic or Inflammatory Lesions

Traumatic and inflammatory lesions develop in an attempt by the body to isolate offending tissue or pathogens in order to maintain homeostasis. This occurs in the entities that are discussed in the next section. The body is miraculous in its attempt to isolate any foreign substance that may threaten homeostasis. The cells perform this feat in several ways. One way is accomplished by the antigen and antibody responses discussed in Chapter 4. In another method, the body's attempt to protect the area of tissue may result in trying to isolate a foreign body from the surrounding tissue through the formation of a **cyst**. The cyst eventually seals the invader off from other tissue.

When inflammation is present, such as an infection of the pulp caused by caries, the epithelium begins to proliferate (grow and reproduce similar cells), form a distinct circle, and eventually close itself off from the surrounding tissue. The **lumen**, or center of the cyst, becomes filled with fluid due to the buildup of osmotic pressure in the core of the cyst. The membrane of the cyst allows fluid to enter the cyst core in an attempt to equalize the osmotic pressure with that of the surrounding tissue, and eventually the cyst expands in size. As bone is resorbed by osteoclasts and bone-resorbing factors, the cyst can expand and continue to fill with fluid and increase in size. **Pseudocysts** have an accumulation of fluid in a cyst-like structure, but they do not have an epithelial lining, so they are not true cysts.

Figure 20.1 is an excellent example of the development of a cyst in its early formation. One of the theories for this development states that inflammation in the bone can stimulate rests of odontogenic epithelium to proliferate and become cystic (Shear, 1992). These rests (small clusters of cells) are termed **epithelial rests**. For this reason, certain cysts such as the **radicular cyst** are known as **inflammatory cysts**. In these cysts, the inflammation comes first and induces epithelial proliferation of the epithelial rests, which have been dormant since tooth development, to begin cyst formation. These remnants become disorganized after tooth development until stimulated by some other force, such as caries or

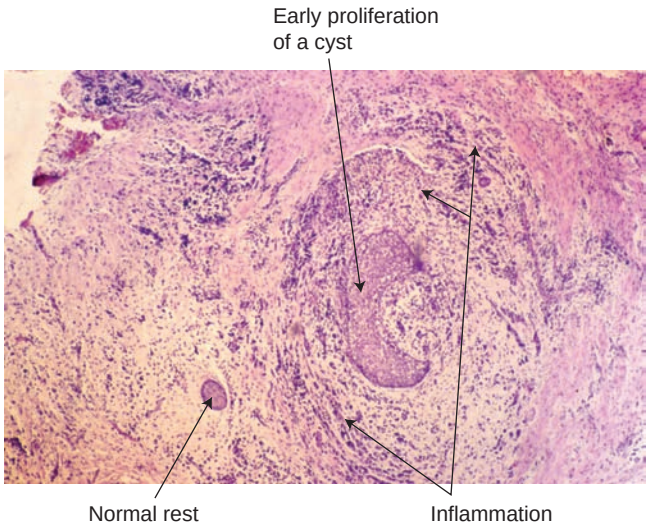


FIGURE 20.1. The formation of a cyst. (Courtesy of Dr. John Jacoway.)

pulpal infection. An example of an inflammatory process is the **dental granuloma**. Figure 20.1 depicts a normal rest without much associated inflammation and then a proliferating rest surrounded by inflammation. This is sometimes called "**precystic" epithelial proliferation**. In other words, the structure of the proliferating rest is associated with inflammation and is growing and beginning to circle in this earliest developmental stage. This cyst originates from the rests of Malassez, which are the remnants of the root sheath of Hertwig, responsible for the formation of the roots of the teeth. The rests have lain dormant until stimulated by a force such as the inflammatory process. Figure 20.2 depicts the location of most odontogenic cysts (those cysts formed from the remnants of the tooth-forming organ) and the inflammatory radicular cyst.

NAME: Periapical granuloma

Etiology: The **periapical granuloma** or dental granuloma (also called apical periodontitis) is the result of necrotic pulp tissue and by-products resulting from an inflammatory process that has damaged the tissue at the apex of the tooth. The infected tissue is the body's defense mechanism coming into action. The periapical granuloma is the first stage of an inflammatory process caused by trauma, injury to the pulp through dental procedures, caries, periodontal disease that has affected the root area severely, or fractures to the tooth. All of these may contribute to the inflammatory process. The process of bone destruction in periapical lesions is not well established, but periapical inflammatory processes result in resorption of bone surrounding the roots of the affected teeth (Menezes et al., 2006).

Method of Transmission: Not applicable

Epidemiology: Any age group may be affected by a periapical granuloma, and there is equal gender distribution. Since it is caused by damage to the tooth structure, anyone may be affected.

Pathogenesis: The diseased tissue from the tooth causes chronically inflamed granulation tissue to accumulate in the

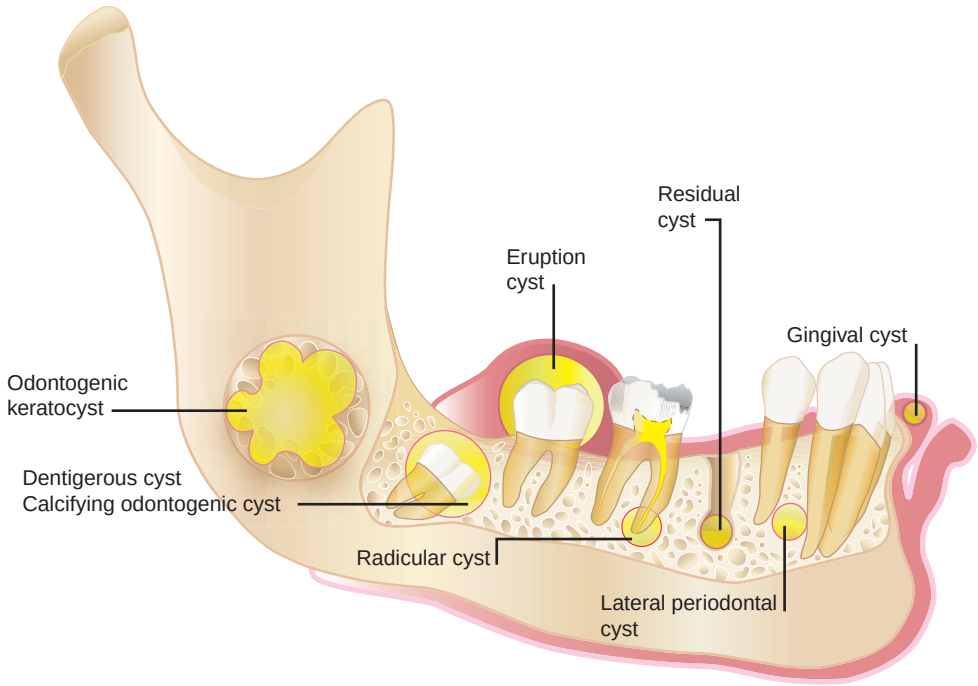


FIGURE 20.2. Location of odontogenic cysts and the radicular cyst.

apical area of the tooth. The mobilizations of host defense mechanisms kill the invading microorganisms and also destroy normal tissue components, inducing bone resorption. As the pulp develops necrosis (cell death or irreversible damage), the tooth may eventually become a **nonvital tooth** (a tooth that has essentially died or is dying because of a pulp that is no longer viable). If chronic inflammation occurs and chemical mediators are present, there may be stimulation of epithelial rests as discussed above. In this case, the granuloma will develop into the radicular cyst as the epithelium begins to separate and wall itself off from surrounding tissue. Reports of the development of periapical granulomas in areas of dental implant placement years after the procedure are published. Stimulation of rests or preexisting long-term residual infection are suggested (McCracken et al., 2012). The bacteria produce toxic products, making the inflammatory process progress in granuloma formation. The granuloma is not the same as the entity that involves granulomatous inflammation, such as those involved in tuberculosis that developed caseous necrosis as the granulomas age. **Caseous necrosis** (see Chapter 2) is a term denoting a necrotic tissue resembling cheese, made of a mixture of protein and fat.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: The periapical granuloma is the accumulation of granulation tissue that is focused at the apical area of a nonvital tooth. The lesion cannot be distinguished from the radicular cyst discussed in the next section, since by all appearances, they are the same radiographically. The tooth may be asymptomatic, but in most cases, complaints such as sensitivity or pain do exist until the tooth becomes completely nonvital. The tooth will test nonvital in most cases, depending upon the degree of damage to the pulp.

Distinguishing Characteristics: The dental granuloma is seen radiographically as a round or ovoid translucent lesion. The size of the lesion may vary from several millimeters to larger, more advanced lesions encompassing larger areas. Figure 20.3 depicts a periapical granuloma at the apex of the anterior teeth with radiolucent, well-demarcated lesions at the apex.

Significant Microscopic Features: The microscopic features of the granuloma are those of inflamed granulation tissue. The inflammatory response consists of a defense mechanism in response to bacterial components. Therefore, there is a lymphocytic infiltrate of plasma cells, neutrophils, histiocytes, foamy macrophages, and eosinophils. The periapical granuloma may be in various stages of development. Omoregie et al. (2011) suggests classifying the periapical granuloma as early, intermediate, or late stage in order to differentiate its development.

FIGURE 20.3. Periapical granuloma. (Courtesy of Dr. John Jacoway.)

Dental Implications: Vitality testing is crucial, since the tooth will test nonvital when obvious radiographic evidence is apparent. If the tooth is nonvital, endodontic treatment is needed. The differentiation of the periapical granuloma and the radicular cyst can only be diagnosed or confirmed by histological examination. Kondori et al. (2011) found that a solely clinical diagnosis (without tissue histology analysis) resulted in a misdiagnosis in 43% of the cases. Periapical granuloma and radicular cysts were two of the most misdiagnosed entities. The authors suggest that any excised lesions should be submitted for a biopsy.

Differential Diagnosis: In a nonvital tooth, a radicular cyst (next section) would be considered.

Treatment and Prognosis: Extraction of the nonvital tooth or endodontic treatment is the usual procedure for granulomas. Apical curettage and apicoectomy may be performed.

APPLICATION 20.1

You have just discovered a radiolucent lesion in the apical area of 27 on Mrs. J. The dentist viewed the radiograph and confirmed that the patient has a probable lateral periodontal cyst, although this would need to be confirmed through biopsy. She is leaving for an extensive trip soon and is worried about this development. Her question to you is what caused the cyst to develop.

Use the material presented in this chapter, including Figure 20.2, to discuss how you would explain to a patient how and why a cyst has developed.

Antibiotic coverage may be needed to get the infection under control. The prognosis is good if all the granuloma is removed.

NAME: Radicular cyst (apical periodontal cyst, periapical cyst)

Etiology: The **radicular cyst** is always associated with a nonvital tooth, and the common causes are caries, trauma such as fracture or injury to the tooth, or periodontal disease. The inflammatory process and necrosis of the pulp cause the epithelial proliferation that a cyst needs to develop. Epithelial rests remain quiescent throughout life but may be stimulated or triggered to proliferate when an inflammatory process develops, such as caries or inflammation of the pulpal tissue.

Epidemiology: The radicular cyst is the most commonly occurring inflammatory cyst of the jaws, with most reported in the maxillary region. Radicular cysts most often are discovered during routine dental examination of radiographs. Studies by Manor et al. (2012), concluded that in a population of 322 patients diagnosed with cystic lesions of the jaw, 155 or 48% were radicular cysts. Radicular cysts or inflammatory cysts tend to be more often found in adults, whereas developmental cysts are more frequently found in children. Results from studies by Jones et al. (2006) indicate that the radicular cyst was the most commonly occurring of all odontogenic cysts in a specimen population of 55,446, of which 7,121 were diagnosed as odontogenic cysts. Similar results were found in 470 cases of odontogenic cysts, with a mean age of 30 years old, male to female ratio of 1.40:1; the most commonly occurring was the radicular cyst followed by the dentigerous cyst (Al Sheddi, 2012). The patient usually reports no pain. Although radicular cysts are the most commonly occurring cysts, the reported incidence varies from less than 50% (Jones et al., 2006; Manor et al., 2012) to as much as 75% of reported cysts. The differentiation of the periapical granuloma (a periapical abscess) and the radicular cyst cannot be made clinically but must be made through biopsy and microscopic interpretation. Jones reported that there was a sharp increase up until the third decade, with a decrease thereafter. Equal gender distribution was also reported.

Pathogenesis: Radicular cysts are derived from the **rests of Malassez,** found in the developing tooth structure of the periodontal ligament. These cells from the rests of Malassez serve as the source of the epithelium that lines the cavities of lesions ultimately becoming a radicular cyst. As discussed above, initially, a granuloma is produced, which then stimulates the cells of the odontogenic epithelial residues or rests within the periodontal ligament (PDL) (i.e., the rests of Malassez). These rests lie dormant until some trigger mechanism such as inflammation causes epithelial proliferation and ultimately, the formation of a cyst.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: The radicular cyst may be found in any region of the mandible and maxilla, but it generally favors the maxillary anterior region at the apex of a nonvital tooth. The patient may experience no pain and is usually not aware of the cyst until it is diagnosed radiographically. The radiograph may show obvious evidence of root resorption (discussed in Chapter 21), depending upon the size and stage of development of the cyst. This type of root resorption appears as a blunting of the root surface,

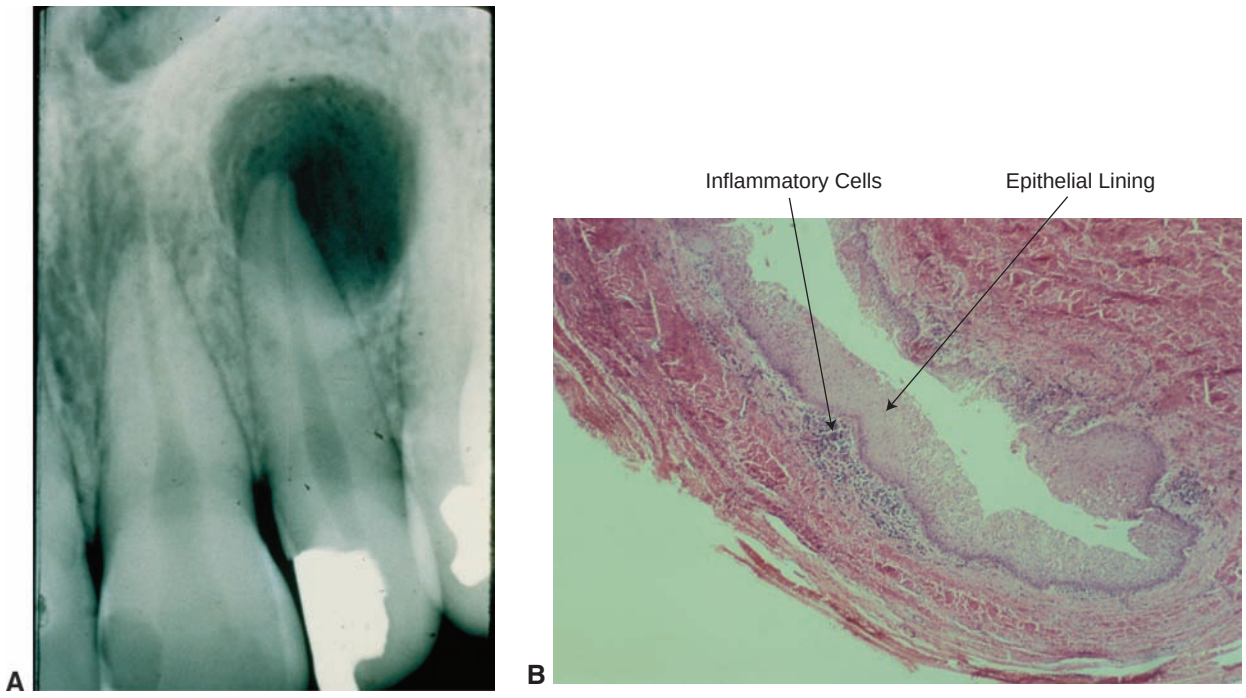


FIGURE 20.4. **A**. Radicular cyst. **B**. Radicular cyst histology. (Both courtesy of Dr. John Jacoway.)

usually at the apices of the tooth. Figure 20.4A depicts the radiographic appearance of a radicular cyst. The radicular cyst appears as a well-circumscribed radiolucent lesion attached to a tooth root. In some cases, the cyst may appear lateral to the apex when a lateral pulp canal is involved.

Distinguishing Characteristics: The radicular cyst cannot be differentiated from the periapical granuloma by a radiograph. A pulp-testing device is used as a diagnostic tool; however, a biopsy is needed to confirm a radicular cyst. If the tooth tests vital, root canal therapy is not indicated; it may also indicate another source for the lesion. Identification can only be made through microscopic examination, since other disease states have very similar radiographic appearances (see differential diagnoses below).

Significant Microscopic Features: The epithelial lining of the radicular cyst is composed of nonkeratinized-stratified squamous epithelium varying in thickness. The lumen may contain necrotic debris and inflammatory infiltrate. Figure 20.4B represents the histology of the radicular cyst, depicting the inflammatory cell infiltrate and the nonkeratinized epithelial lining.

Dental Implications: Failure to remove the radicular cyst completely results in recurrence.

Differential Diagnosis: The radicular cyst is usually discovered on a radiograph, but the radiolucent characteristics are not diagnostic, since other entities may appear similar. Periapical central giant cell granulomas are sometimes misdiagnosed as radicular cysts (Lombardi et al., 2006).

1. Periapical granuloma, Chapter 20
2. Central giant cell granuloma, Chapter 18
3. Newly developing periapical cementoosseous dysplasia, Chapter 20
4. Traumatic bone cysts (when in the posterior region), Chapter 20

Treatment and Prognosis: Treatment usually involves several options: removal by extraction, surgery with curettage, and root canal therapy. Treatment may also include surgery and apicoectomy. Antibiotic coverage may be needed to get the infection under control. The prognosis is good with complete removal. Failure to remove the entire cyst results in what is called a **residual cyst.** This cyst develops after the stimulating inflammatory products have been removed. The cyst can produce extensive weakening and invasion of the bone. If fragments remain, the residual cyst may be a concern.

NAME: Aneurysmal bone cyst

Etiology: The **aneurysmal bone cyst** is considered a pseudocyst, in that it appears as a cyst, but unlike the epithelium-lined true cyst, the aneurysmal bone cyst does not have the epithelium-lined lumen. This lesion is a benign lesion that is blood filled. It is suggested that this type of bone cyst arises from prior trauma, and recent research suggests some genetic components (Leithner et al., 2004). Cytogenetic research suggests chromosomal alterations. Some literature suggests that it may well be a tumor rather than a reactive lesion. However, this is still under consideration and research.

Method of Transmission: Not applicable

Epidemiology: Aneurysmal bone cysts are found in individuals less than 30 years of age, with a peak incidence in the second decade of life (Rapp et al., 2012). The bone cysts are rare and account for about 1 to 2% of primary biopsies on bone tumors (Perrotti et al., 2004). A slight female predilection is common. The mandible is more involved than the maxilla, and they are more common in the posterior regions of the mouth. However, most occur in the long bones or vertebral column; occurrence in the jaws is rare, accounting for only 1.5% of all nonodontogenic and nonepithelial cysts of the jaws (Behal, 2011).

Pathogenesis: The pathogenesis is unclear about whether there is a preexisting lesion or whether the bone cyst develops because of dilated vessels. Also discussed is the association with hematomas as a causal agent. The venous pressure may increase and cause expansion.

Extraoral Characteristics: Extraoral swelling is reported in extensive lesions.

Perioral and Intraoral Characteristics: The patient usually notices swelling with or without pain. The radiographic features of an aneurysmal bone cyst include a unilocular or multilocular lesion, described as having a "soap bubble" appearance. Thinning and expansion of the cortical bone may be seen. Ballooning and distention of the cortical bone is often recognized and depending upon the stage of the cyst, the appearance will vary. Figure 20.5 demonstrates the honeycomb or soap bubble appearance of the aneurysmal bone cyst.

Distinguishing Characteristics: Aneurysmal bone cysts exhibit some key radiographic appearances as described above. The lesion presents as expansile, with thin peripheral bone that is blood filled, without the presence of what is called bruit (a purring sound at the suspected area of aneurysmal cyst), thrill (a vibration), or pulse pressure (Rattan & Goyal, 2006). A vascular type of lesion has a pulse sensation. If such a sensation is present, then a change in a differential diagnosis is needed.

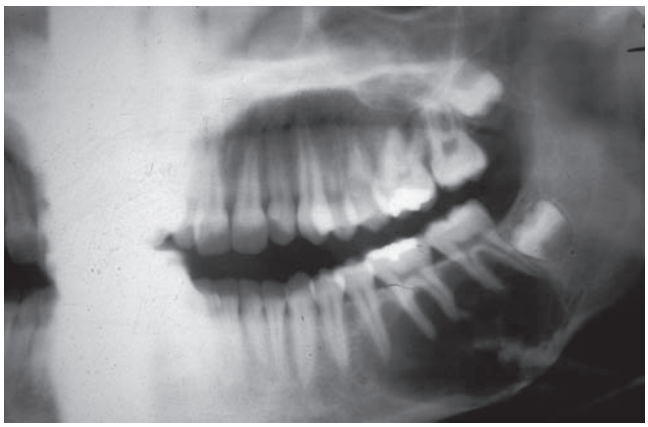


FIGURE 20.5. Aneurysmal bone cyst. (Courtesy of Dr. Shabnum Meer.)

Significant Microscopic Features: The nonepithelial lining is composed of immature connective tissue and scattered multinucleated giant cells. A thin layer of a bony shell often covers the blood-filled cavity.

Dental Implications: Aneurysmal bone cysts may cause the teeth to become displaced or loose because of bone expansion.

Differential Diagnosis: The prime considerations because of the radiographic appearance are:

1. Odontogenic keratocyst, Chapter 20
2. Central giant cell granuloma, Chapter 18
3. Ameloblastic fibroma, Chapter, 20
4. Ameloblastoma, Chapter 18

Treatment and Prognosis: Excision and curettage is the treatment of choice. When the lesion is removed completely, the prognosis is good. Cryotherapy, sclerotherapy, radionuclide ablation, and en bloc resection may be used for certain cases. There may be recurrence if any lesion remains, and the rate of this recurrence is usually very high.

NAME: Traumatic bone cyst

Etiology: **Traumatic bone cyst** (also called simple bone cyst) is as the name implies; that is, it is thought to be caused by trauma. However, studies question whether this is true with little supporting evidence in the literature to suggest trauma as a sole etiology. This cyst is not considered a true cyst because it is not epithelium lined.

Method of Transmission: Not applicable

Epidemiology: The traumatic bone cyst is usually found in the 10- to 20-year-old age group, although they have also been reported in a wide range of ages. There is no gender preference. The most common site for a traumatic bone cyst is in the mandible (Dvori et al., 2006).

Pathogenesis: The traumatic bone cyst was originally thought to be a hematoma (Chapter 13), probably induced by trauma, which does not heal and subsequently liquefies and becomes a cyst. Since it is not epithelium lined, it fits more in the category of a pseudocyst. Another cause that has been suggested is calcium deficiency.

Extraoral Characteristics: The traumatic bone cysts may cause extraoral swelling if the lesion is large enough or has existed long enough.

Perioral and Intraoral Characteristics: Increased swelling in the mouth may be observed, but pain is not usually a factor. The lesions are discovered on radiographs, with the patient reporting no pain or other symptoms. The radiographic appearance is that of a scalloping cyst with well-delineated radiolucent characteristics. Margins may be very sharp in some areas and ill defined in others. The cyst is also often seen scalloping between the teeth. Figure 20.6 depicts a traumatic bone cyst in a large area of the mandible, manifesting a scalloped appearance that reaches between the teeth in a honeycomb radiographic appearance.

FIGURE 20.6. Traumatic bone cyst. (Courtesy of Dr. Shabnum Meer.)

Distinguishing Characteristics: When questioning the patient about a radiolucent lesion, the patient will often report previous trauma to the area in question. When the lesion is opened, the escape of blood from the lesion indicates that it was blood filled, which suggests a traumatic bone cyst. Pain is not a commonly reported factor.

Significant Microscopic Features: When viewing the traumatic bone cyst, an epithelial component is not present, since there is no epithelial lining. Bone and blood products are generally seen.

Dental Implications: The traumatic bone cyst may continue to expand and increase in size when not detected in the early stages. The lesion must be drained to begin healing.

Differential Diagnosis: Cases have been reported of florid cementoosseous dysplasia (COD) (discussed in Chapter 20) as a differential diagnosis in connection with these types of lesions.

Treatment and Prognosis: The usual treatment involves opening the cyst. Once the blood cavity is emptied, the bone will repair itself over time. There is a good prognosis with no recurrence.

NAME: Cementoosseous dysplasia

Cementoooosseous dysplasia (COD) is usually discovered during a radiographic examination. The patient will usually not report any sensitivity or discomfort. The terms "cementoosseous dysplasias" represents three types of lesions that are believed to fall under this heading and are variants of the same category (World Health Organization, 2005). These variants include:

1. **Periapical cementoosseous dysplasia** (formerly referred to as **cementoma**) occurs in the apical area of the teeth, usually in the lower anterior region of middle-aged black women. The teeth will test vital.
2. **Focal cementoosseous dysplasia** most commonly occurs in the posterior mandible region. It is most commonly found in whites, but may occur in other ethnicities as well.
3. **Florid cementoosseous dysplasia** may cover a wide area of involvement in both jaws. Patients are more likely to report this form as producing symptoms such as a dull pain. Generally, this entity affects blacks, Asians, and whites. This variant must be differentiated from Paget disease, chronic diffuse osteomyelitis, and Gardner syndrome. The differentiation of simple bone cysts and secondary infection or osteomyelitis may make the determination more difficult.

The three variations are discussed below.

Etiology: The etiology of these lesions is unknown, but they are considered a reactive process. There may be a familial trait as reported by Kim et al. (2011).

Method of Transmission: Not applicable

Epidemiology: Periapical COD is a reactive process that is not contagious and is considered benign. Occurrence is usually in the over 40-year-old age group and usually around middle age. Women are affected most often, particularly middle-aged black women (Regezi et al., 2003). Recent retrospective studies by Alsufyani and Lam (2011), found demographics in a study population of 117 patients to consist of women (82.9% or 97 patients) in the fifth decade of life who presented with asymptomatic OD/COD.

Pathogenesis: Some researchers suggest that cementoosseous dysplastic conditions are developmental and related to a defect in the bone and/or cementum remodeling in adulthood, and others consider them only reactionary type entities.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: The patient is usually asymptomatic, and the lesions are discovered on routine radiographs. Figure 20.7A shows the progression of periapical COD over a 23-year period.

Distinguishing Characteristics: Periapical COD occurs at the apex of vital teeth, with a propensity for the anterior

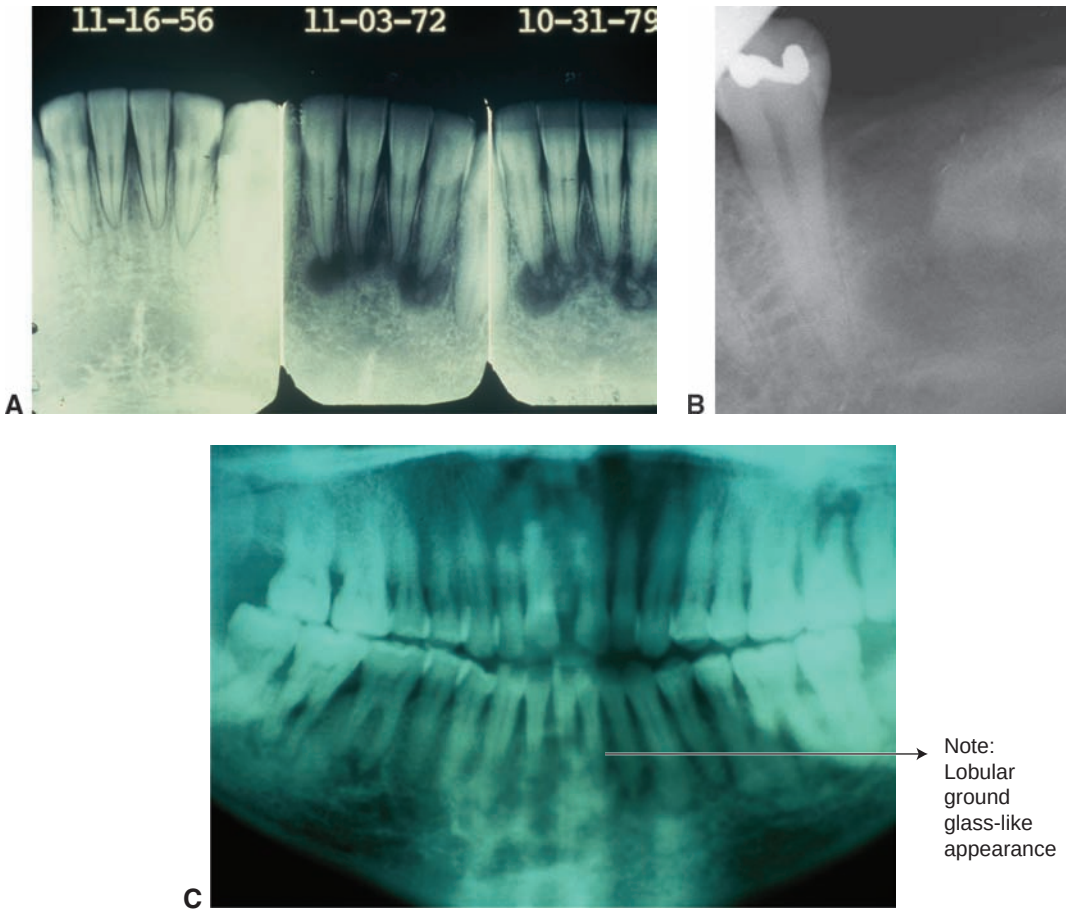


FIGURE 20.7. **A**. Progression of peripheral cementoosseous dysplasia (cementoma). (Courtesy of Dr. E.J. Burkes, Jr.) **B**. Focal osseous dysplasia. (Courtesy of Dr. Enrique Platin.) **C**. Florid cementoosseous dysplasia. (Courtesy of Dr. Michael Brennan.)

mandibular teeth. The cementoma is asymptomatic and not usually noticed until seen on a radiograph.

Significant Microscopic Features: The histology of the periapical COD is that of fibrous connective tissue that can be seen with bone and cementum in varying quantities. The three types of COD are indistinguishable histologically.

Dental Implications: The vitality of the tooth is important, since the tooth tests vital with periapical COD (Komabayashi & Zhu, 2011). Without the proper diagnostic procedure, the tooth may be treated with a root canal when this is not necessary.

Differential Diagnosis: The diagnosis of periapical COD depends upon the stage in development of the lesions. The initial diagnosis is important, since in the early stages, there may be a radiolucent appearance that would appear more cyst-like and, histologically, may appear as bone dysplasia. As the lesion calcifies and becomes more opaque, the lesion may appear more as a tumor. Additional considerations are:

1. Odontoma, Chapter 19
2. Cementoossifying fibroma, Chapter 17

Treatment and Prognosis: Periapical COD requires no treatment, and extraction or surgery is not required since the teeth remain vital. Early recognition and determination will alleviate unnecessary tests and surgery (Alsufyani & Lam, 2011) (Wright, 1999).

Focal Cementoosseous Dysplasia. **Focal COD** is believed to be closely related to periapical COD, with most experts claiming that they are indeed variants of the same entity. Most cases occur in females around the fourth to fifth decade of life. In contrast to the periapical COD, the focal COD occurs most often in whites rather than blacks (Neville et al., 1999). The term "focal" is used when the lesion occurs in areas other than at the apex of the tooth as shown in Figure 20.7B. The lesion is described as a solitary, unilateral lesion that is well defined, with a radiolucent border surrounded by a radiopaque border and most are mixed radiolucent and radiopaque entities. The lesions can also be radiolucent, progressing in time to a more radiopaque, lesion (Alsufyani & Lam, 2011). Again, just as generally occurs with the periapical COD lesion, the focal version is usually discovered on a radiograph and is asymptomatic.

Florid Cementoosseous Dysplasia. **Florid COD** mostly affects adult black women and Asian women and a familial tendency is reported (Singer et al., 2005; Kim et al., 2011). The disorder can affect any quadrant of the mouth and is sometimes seen in all quadrants at the same time. Clinically, there may be evidence of a yellow bone-like material, and during surgical removal, it is difficult to separate the material from the bone. The radiograph may have a more "ground glass" type of appearance as seen in Figure 20.7C.

The radiographic appearance of florid COD is one of progressing lucent and opaque quality, which is described as lobular. The differentiation between florid COD and simple bone cyst is not readily distinguishable, and in some cases, a bone cyst is reported when in actuality, it was a florid COD with secondary infections. The treatment is through observation, clinical recalls, and prophylaxis. Osteomyelitis can be a complication in severe cases. Differential diagnosis may include:

1. Paget disease, Chapter 10
2. Osteomas of Gardner syndrome, Chapter 19
3. Simple bone cyst, Chapter 20
4. Chronic diffuse osteomyelitis, Chapter 19

Infections

Infections of the mouth can be extensive enough to penetrate into the bone. Many are caused by periodontal problems, fractures, breaks in the mucosa, and bacteria that enter the bone. Two types of infections discussed in this section are acute osteomyelitis and chronic osteomyelitis.

Acute osteomyelitis exhibits an acute inflammatory response with the general signs of an inflammatory process. The patient may complain of pain and swelling with lymphadenopathy. Chronic osteomyelitis results when acute osteomyelitis is not resolved.

NAME: Osteomyelitis—acute and chronic forms

Etiology: A periapical abscess is most often the cause of the acute form of **osteomyelitis.** There may be specific bacteria involved in the occurrence, such as staphylococci, actinomyces, and streptococci. Fractures, trauma, and surgery including extractions (see Chapter 3 covering alveolar osteitis) can also allow bacteria to enter the bone. If the acute form is not addressed completely, the chronic form usually follows. The chronic form may additionally be caused by a long-term inflammatory reaction from some stimulus, such as a systemic disease affecting the bone. Most cases of osteomyelitis are infectious, and any organism may be involved. Bone radiated for head and neck cancer is especially susceptible to osteonecrosis (see Chapter 5). The decreased blood supply and radiation exposure to the bone places the patient at a high risk for infections.

Method of Transmission: The acute form of osteomyelitis may have several infectious organisms involved in the disease process (see Pathogenesis, below).

Epidemiology: Osteomyelitis can occur in any age group. Both sexes are equally affected.

Pathogenesis: Staphylococci and streptococci are the bacteria most commonly involved in the origin of osteomyelitis. The difference between acute and chronic osteomyelitis is often the virulence of the bacteria involved. Acute osteomyelitis is always destructive and painful.

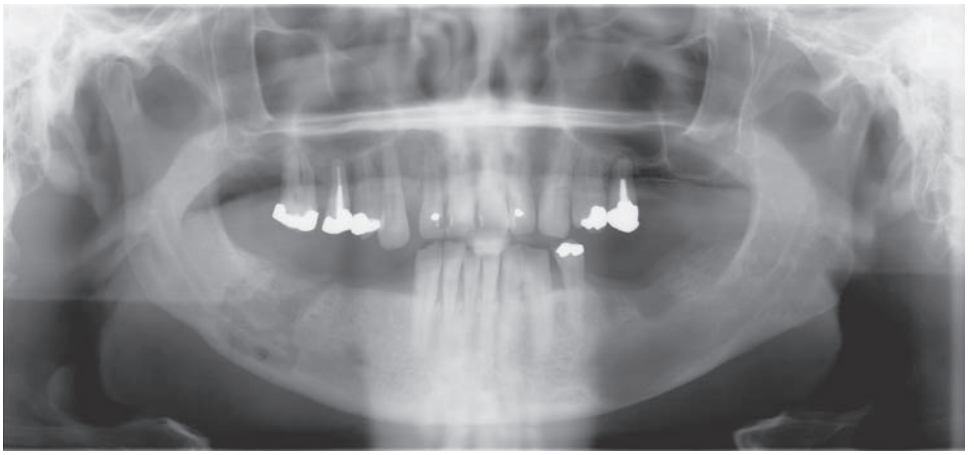


FIGURE 20.8. Panoramic radiograph showing osteomyelitis. (Courtesy of Dr. Michael Bornstein.)

Extraoral Characteristics: Lymphadenopathy, fever, and pain are often symptoms of osteomyelitis and are especially noted in the acute form.

Perioral and Intraoral Characteristics: An acute infection may not produce the destruction that the chronic form produces, because it has not been present long enough to create bone damage. In the chronic form, more evident patches of necrotic bone and diffuse radiolucent lesions are seen, and the lesions appear more mottled, with a sclerotic appearance on the radiograph. Figure 20.8 shows osteomyelitis in the posterior molar region.

Distinguishing Characteristics: The radiographic appearance is a distinguishing characteristic.

Significant Microscopic Features: The specimen shows loss of osteocytes from their lacunae and bacterial colonization with the presence of predominately necrotic bone. Abscess formation occurs containing **sequestrum** (necrotic bone that has broken away from the vital bone; pl., sequestra).

Dental Implications: The patient may have pain and lymphadenopathy. Addressing the cause of the osteomyelitis is paramount. The correct antibiotic is needed to treat the infection; therefore, identification of the specific organism through laboratory tests is crucial.

Differential Diagnosis: The pain, lymphadenopathy, and radiographic appearance usually indicate osteomyelitis. The clinical appearance along with the existence of an open area allowing bacteria to enter the site, such as occurs with caries or in extraction sites, allow a more definitive diagnosis.

Treatment and Prognosis: Drainage and antibiotics are needed to treat the acute form of osteomyelitis. The chronic form is more difficult to manage because of necrosis. Surgery is indicated, with antibiotic coverage. In acute osteomyelitis, antibiotics are very effective, but chronic osteomyelitis usually requires surgery, antibiotics, and drainage.

Developmental Cysts

As mentioned in the beginning of the chapter, a cyst is defined as an epithelium-lined cavity that contains a serous or semisolid material. The odontogenic cyst arises primarily

APPLICATION 20.2

Reports of osteomyelitis linked to bisphosphonate use (see Chapter 10) have continued to increase and have become an issue with many dental patients. Bisphosphonates are used in the management of metastatic disease and in the treatment of osteoporosis (Nase & Suzuki, 2006; Soolari & Soolari, 2011). Reports indicate a rise in osteonecrosis of the jaws associated with these medications; thus as this usage continues to increase, the clinician may see more cases related to osteomyelitis in the dental office (Ruggiero et al., 2004). Diz et al. (2011) point out that, as the population continues to age, treatment for osteoporosis will increase and so may oral bisphoshonate–related osteonecrosis of the jaw. The goal of research related to this crises is to help identify osteonecrosis in patients early and prevent advancement of damage to the bone (Otomo-Corgel, 2006).

In addition to the new focus on bisphosphonates, cases of methicillin-resistant *Staphylococcus aureus* (MRSA) infection are also being reported, and this organism has been known to affect any bone (Arnold et al., 2006; CDC, 2011). As the name implies, concern exists regarding the currently available antimicrobial agents and the fact that they may become ineffective in treating systemic infections, including osteomyelitis. This could be a concern when osteomyelitis affects the maxillae and mandible (Appelbaum, 2006). With third molar extractions, implants, and other penetrations within the bone, this could be a very real possibility, especially if the patient reports previous episodes with MRSA.

in the soft tissue and bone (see Fig. 20.2). Traumatic and inflammatory lesions and infections have been discussed up to this point; developmental cysts are the topic of this section.

NAME: Lateral periodontal cyst (botryoid odontogenic cyst)

Etiology: **Lateral periodontal cysts** are odontogenic, nonkeratinized developmental cysts, believed to develop from the dental lamina remnants (rests of Malassez) from within bone.

Method of Transmission: Not applicable

Epidemiology: The lateral periodontal cyst is usually found in individuals in the third decade of life and beyond, and there is a male predilection. The mandibular premolar and cuspid area is favored, followed by the maxillary premolar and cuspid region. In a study by Jones et al. (2006), data from 55,446 specimens were reviewed, and 7,121 specimens were odontogenic cysts. Lateral periodontal cysts represented 0.4% of the diagnosed cysts, with an average age of 48.2 years.

Pathogenesis: The lateral cyst is found mostly in the mandibular cuspid and premolar region on the lateral surface of the tooth.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: The lateral periodontal cyst is asymptomatic in most cases and is not usually noticed until seen on a radiograph. The cyst is usually unilocular, round or oval, and is well-delineated. Figure 20.9A shows a lateral periodontal cyst.

Distinguishing Characteristics: The teeth associated with the lateral periodontal cyst are vital. When a multilocular cyst is present, it is called a variant of the lateral periodontal cyst and is known as the **botryoid odontogenic cyst**. Siponen et al. (2011) state that it might be that several adjacent epithelial rests simultaneously undergo cystic change and eventually form a polycystic lesion. In their recent paper, four cases are presented.

Significant Microscopic Features: The thin lining of the cyst consists of cuboidal epithelium. The cyst demonstrates clusters and whorls of cells, some of which have clear cytoplasm (clear cells).

Dental Implications: The cyst should be identified as a lateral periodontal cyst, since it is necessary to rule out an inflammatory-type lesion or a more serious type of cyst or tumor, such as the odontogenic keratocyst (OKC) discussed below in this chapter.

Differential Diagnosis: When occurring in the lateral location of premolars and cuspid area, the following are considerations:

1. Radicular cyst, Chapter 20
2. Odontogenic keratocyst, Chapter 20

Treatment and Prognosis: Surgical excision and pathologic review is the treatment of choice. Vitality testing is important in order to avoid unnecessary endodontic treatment. There may be a higher rate of recurrence when the cyst is a botryoid odontogenic cyst. Periodic radiographic follow-up is needed. The prognosis is excellent.

Gingival Cyst of the Adult. The **gingival cyst of the adult** is the soft tissue counterpart to the lateral periodontal cyst. Both the gingival and the lateral periodontal cyst are developmental cysts. Since the occurrence is approximately 0.15% of submitted specimens, Bell et al. (1997) suggests that most clinicians may not have encountered the gingival cyst of the adult. However, it is thought that misdiagnosis may occur and the lesion may be diagnosed as a mucocele because of the similar appearance clinically. The gingival cyst may occur at a later age, around the fourth through sixth decade of life, occurring predominately in the mandible 60% of the time, with a slight female predilection (Jones et al., 2006; Kelsey et al., 2009). The cyst presents as a firm, flesh-colored nodule that is painless, nonmobile, and usually measures 1 to 3 mm in diameter, although some may be larger. The teeth in the

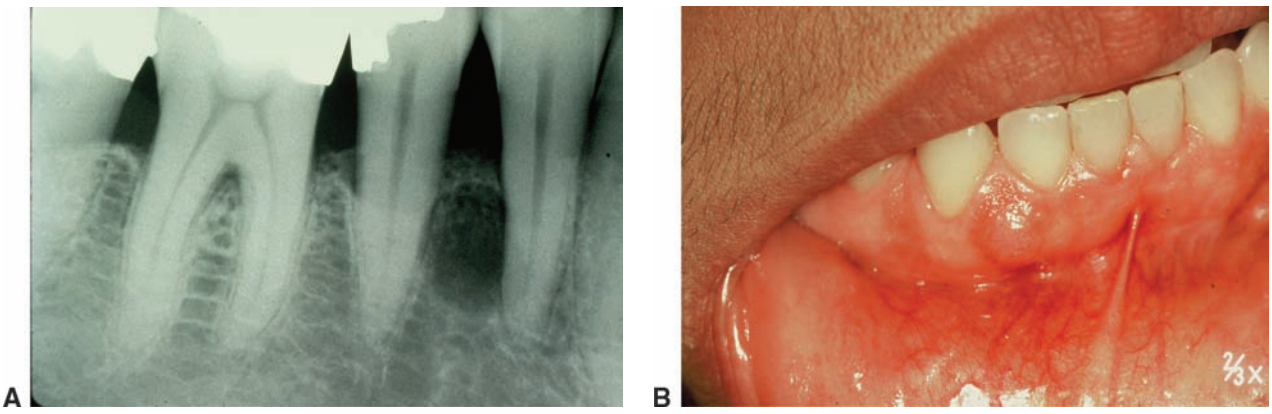


FIGURE 20.9. **A**. Lateral periodontal cyst. (Courtesy of Dr. Carolyn Bentley.) **B**. Gingival cyst in an adult. (Courtesy of Dr. John Jacoway.)

area test vital unless previous damage from other sources has occurred that damage the pulp. The **rests of Serres** (originating from the dental lamina, occurring from the epithelial connection between the mucosa and the enamel organ) is believed to be the source for the gingival counterpart to the lateral periodontal cyst when trapped within the soft tissue (Regezi et al., 2003). Other explanations include the remnants of the reduced enamel epithelium/junctional epithelium or remnants of the cell rests of Malassez. The lining of the cavity may be squamous, cuboidal, or in some cases, columnar and classically only three layers thick with occasional focal thickenings (Bell et al., 1997). The cells of the gingival cyst of the adult may exhibit a clear, glycogen-rich cytoplasm. Figure 20.9B shows the gingival cyst. A differential diagnosis may include: lateral periodontal cyst, peripheral giant cell granuloma, mucocele, and odontogentic keratocyst. Treatment consists of surgical excision and histopathologic examination. Alveolar defects may be noted upon removal of the growth that may not be evident initially in a radiograph (Kelsey et al., 2009).

NAME: Dentigerous cyst

Etiology: **Dentigerous cysts** are odontogenic in development and arise from a cystic change in the dental follicle following crown formation. The reduced enamel epithelium results from the remnants of the enamel organ. The dentigerous cyst is always associated with the crown of an impacted or unerupted tooth, supernumerary tooth, or odontoma.

Method of Transmission: Not applicable

Epidemiology: The dentigerous cyst is the second most commonly occurring odontogenic cyst, following the most common radicular cyst. However, dentigerous cysts are the most commonly occurring developmental cysts of the jaw. Dentigerous cysts are usually found in a young age group, especially in those with unerupted third molars. Dentigerous cyst development around tooth buds of premolars has been reported in the very young, including a 6-year-old child (Bozdogan et al., 2012). Reports by Jones et al. (2006) found that 81.6% of the cysts in a patient population of 1,292 diagnosed with dentigerous cysts developed in the mandible region. The remainder occurred in the anterior maxilla. A male gender preference was reported at 1.86 to 1.

Pathogenesis: Dentigerous cysts are also known as follicular cysts and are found around the crown of unerupted third molars, canines, and unerupted teeth. The cyst has an accumulation of fluid between the completely formed crown of a tooth and the reduced-enamel epithelium. The attachment is at the cementoenamel junction.

The **paradental cyst** is derived from the enamel epithelium and is thought to be a variant of the dentigerous cyst. An enamel projection is present in the bifurcation area of the third molars, which is thought to stimulate cyst production. The histology is similar to that of the dentigerous cyst with some inflammation. The appearance is often observed, and the prime areas are third molars for adults and unerupted first molars in children; however, other posterior teeth may be involved as well. Extraction of a third molar with curettage of the cyst is performed with close follow-up.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: The dentigerous cyst is usually only evident on radiographs, with no symptoms of pain or discomfort reported. On radiographs, it is well circumscribed, unilocular, and sometimes multilocular. Figure 20.10A shows a dentigerous cyst around an impacted tooth. Figure 20.9B shows a dentigerous cyst in the distal area of a third molar.

Distinguishing Characteristics: On radiograph, the dentigerous cyst is well circumscribed, unilocular, and sometimes multilocular. Since there is no calcified material, the cyst appears completely radiolucent.

Significant Microscopic Features: The thin lining of the dentigerous cyst is composed of stratified squamous epithelium, varying in thickness, which is usually a few cell layers thick. The epithelial lining is nonkeratinized. Some lining may contain mucous cells and/or ciliated columnar respiratory-type epithelium. The fibrous connective tissue wall varies in thickness and may exhibit inflammation. Odontogenic epithelium or dental lamina remnants may be seen as well. Figure 20.10C shows the histology of a dentigerous cyst with a cyst lining of epithelial tissue several layers thick.

Dental Implications: Delayed tooth eruption is a common theme. The dentigerous cyst can become quite large and has the potential to displace teeth and resorb roots. Dentigerous cysts continue to grow and expand; therefore, early diagnosis is imperative.

Differential Diagnosis: Other possible lesions to consider are:

1. Odontogenic keratocyst, Chapter 20
2. Ameloblastoma, Chapter 18
3. Adenomatoid odontogenic tumor, Chapter 20

Treatment and Prognosis: Complete removal of the cyst is indicated, since the recurrence is high when this is not fully accomplished. The prognosis is excellent, but the patient should be followed closely, since a slight possibility for subsequent tumors, such as the ameloblastoma or mucoepidermoid carcinoma, exists.

NAME: Eruption cyst

Etiology: The **eruption cyst**, sometimes called an eruption hematoma, is considered a variant of the dentigerous cyst and is caused by the accumulation of fluid or blood between the crown of an erupting tooth and the reduced enamel organ, due to trauma.

Method of Transmission: Not applicable

Epidemiology: The eruption cyst is not gender specific. Most occur in deciduous teeth and permanent molars of children (Sciubba et al., 2001).

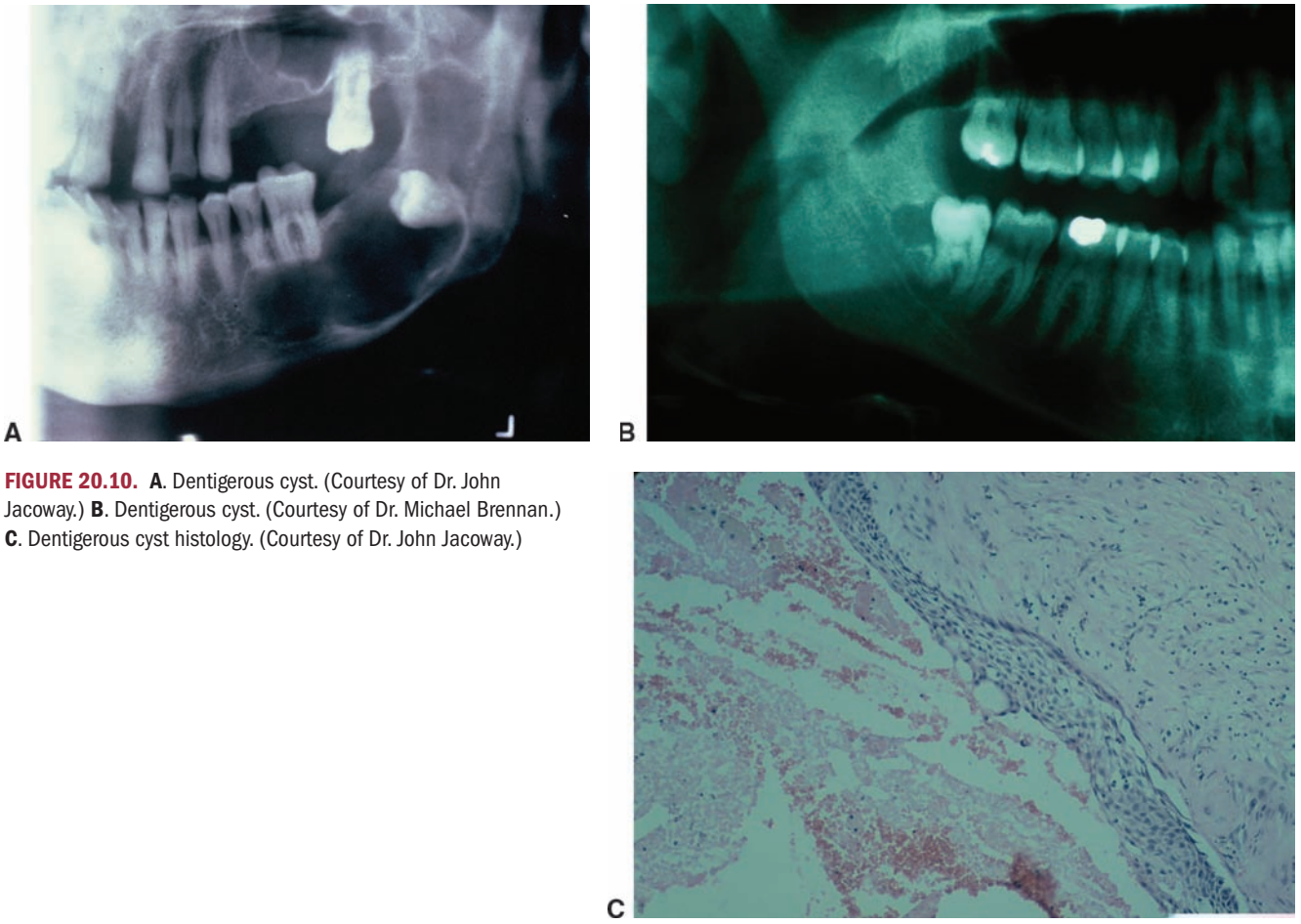


FIGURE 20.10. **A**. Dentigerous cyst. (Courtesy of Dr. John Jacoway.) **B**. Dentigerous cyst. (Courtesy of Dr. Michael Brennan.) **C**. Dentigerous cyst histology. (Courtesy of Dr. John Jacoway.)

Pathogenesis: The eruption cyst is usually painless and is found around the crown of an unerupted tooth. The cysts are probably unreported in most cases, since the cyst will rupture following eruption of the relevant tooth.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: The tissue of the eruption cyst may have a darker appearance and appear elevated. The eruption cyst is seen as a smooth bluish swelling (dome-like) on the crest of the alveolar ridge. The radiographic finding of an eruption cyst is an enlarged follicular space.

Distinguishing Characteristics: The cysts may have a bluish cast due to the inflammatory inner core and blood accumulation. Figure 20.11 shows an eruption cyst. Note the blue hue of the lesion.

Significant Microscopic Features: The microscopic feature is a blood- and fluid-filled cavity. Normal oral mucosa on the surface is found with cyst epithelium containing heavy inflammatory infiltrate covering the inner aspect.

Dental Implications: The only dental implication is the failure of the tooth to erupt; therefore, the cyst may be opened to hasten the event. Most eruption cysts are left to dissipate on their own.

Differential Diagnosis: The radiograph of the area confirms the pending tooth eruption, and the eruption cyst around the tooth.

Treatment and Prognosis: No treatment is necessary; however on occasion, removal of the overlying tissue could facilitate a quicker eruption. The tooth eventually erupts through the tissue, and the cyst disappears.

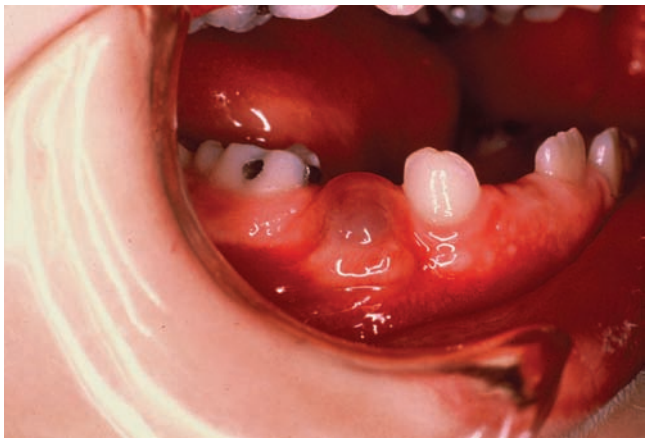


FIGURE 20.11. Eruption cyst. (Courtesy of Dr. John Jacoway.)

Gingival Cyst of the Newborn (Bohn Nodules or Dental Lamina Cysts of the Newborn). Another consideration with regard to the clinical appearance of eruption cysts is the gingival cysts that occur on the ridges of the oral tissues in the newborn **(Bohn nodules)**. The nodules are multiple small cysts found at the junction of the hard and soft palates and along buccal and lingual dental ridges. The nodules usually disappear and rupture over time and are of no concern. The usual clinical scenario is the worried mother who believes that her baby's teeth are erupting too early and seeks evaluation. Epstein pearls or palatine cysts of the newborn are similar developmental cysts occurring in the line of fusion in the midline of the palate. They are inclusion cysts and require no treatment.

NAME: Odontogenic keratocyst

Etiology: The **odontogenic keratocyst (OKC)** develops from the dental lamina or its remnants. It is a developmental cyst and very aggressive.

Method of Transmission: Not applicable

Epidemiology: The OKC is three times more common in the mandible. In a study by Jones et al. (2006), the lesion occurred in the mandible in 96% of the cases in which the site of presentation was known. In an evaluation of 55,446 specimens submitted over a 30-year period (Jones et al., 2006), it was calculated that 828 were odontogenic cysts, with 464 in males and 364 in females, a ratio of 1.27 to 1. The age group affected ranged from 5 years to 92 years, with an average age of occurrence at 41 years. The OKC is the third most commonly occurring odontogenic cyst, preceded by the radicular cyst (seen most frequently) and the dentigerous cyst (the second most common).

Pathogenesis: The source of the OKC is the dental lamina; the epithelial rests of Malassez and Serres are suggested as well.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: OKCs occur most often in the posterior mandibular region and can occupy most of the ramus in some cases. In late stages of development the cyst may become large enough to displace teeth and extend through the cancellous bone into the oral cavity. As the jaw becomes weakened, a fracture is more likely to occur.

Radiographically, the lesions can be multilocular or unilocular, well circumscribed on the radiograph, and radiolucent, with a scalloped appearance. The radiographic appearance closely resembles that of an ameloblastoma in certain cases. They can also be round and ovoid and appear laterally to the tooth, making them appear as a lateral periodontal cyst (Singh & Gupta, 2010). Figure 20.12A shows an OKC in the ramus. Figure 20.12B shows an OKC, and Figure 20.12C depicts the histology of the keratocyst.

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: The basal cell layer may be cuboidal or columnar. The basal cell layer has hyperchromatic nuclei, and the corrugated surface is parakeratinized and in some cases orthokeratinized. The parakeratinized cysts may occur more often because of the thin, friable fibrous capsule. In most cases, there is epithelial budding and the existence of daughter cysts (islands of epithelium). The OKCs that are associated with nevoid basal cell carcinoma (BCC) syndrome, discussed next in this chapter, tend to have more daughter cysts or satellite cysts; the recurrence rate is higher because of this fragmented cellular proliferation. The lumen of the cyst is filled with keratin.

Dental Implications: Although the OKC can radiographically resemble other cysts, the microscopic interpretation is unique once a specimen is submitted. The association with nevoid BCC syndrome is especially important in a diagnosis, and the cysts have very aggressive behavior. Therefore, prompt treatment is required.

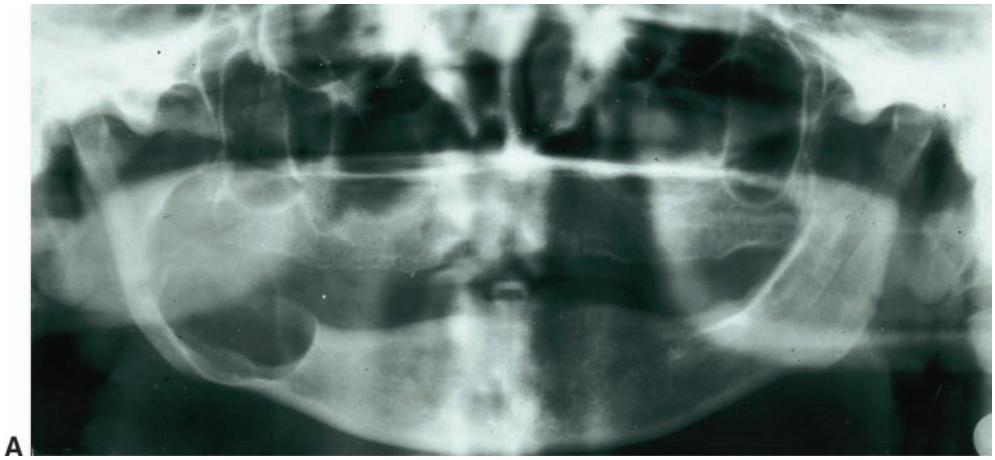
Differential Diagnosis: When associated with teeth, the following are considerations:

1. Radicular cyst, Chapter 20
2. Dentigerous cyst, Chapter 20
3. Ameloblastoma, Chapter 18
4. Adenomatoid odontogenic tumor, Chapter 20
5. Central giant cell granuloma, Chapter 18
6. Lateral periodontal cyst, Chapter 20
7. Traumatic bone cyst, Chapter 20

Treatment and Prognosis: Since recurrence is high (as much as 60%), careful removal of the entire structure is crucial, and the capsule must be removed intact so that daughter cells do not remain. Recurrence usually takes place in the first 5 years after removal.

Nevoid Basal Cell Carcinoma Syndrome (Gorlin-Goltz Syndrome). Also known as Gorlin-Goltz syndrome, (Gorlin & Goltz, 1960), **nevoid basal cell carcinoma syndrome** is a prime concern for patients diagnosed with OKC due to a close association between the two disorders. This syndrome is an inherited autosomal dominant disorder with a male predilection of 3 to 1 (Melo et al., 2004). The syndrome affects approximately 1/57,000 to 1/256,000 individuals. The syndrome has five main components: nevoid BCC (10 or more), jaw cysts, congenital skeletal anomalies (bifid fused rib or vertebrae, ectopic), calcifications, and palmar and plantar pits. The patient will have nevi or small basal cell carcinomas on cutaneous areas, as shown in Figure 20.13 A. The face is affected most often, followed by the chest area, and the hereditary disorder is seen more often in whites (Sirous & Tayari, 2011). In a group of patients studied by Evans et al. (1993), 75% of patients over 20 years of age had BCC and 90% of those over 40 years of age had BCC. The acceleration seems to occur in the third decade.

Additionally, there are other reported characteristics associated with this disease including a wide nasal



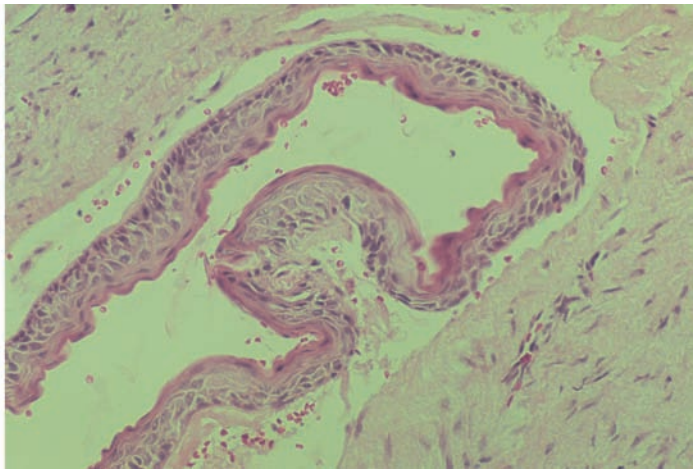


FIGURE 20.12. **A**. Radiograph of odontogenic keratocyst (OKC). (Courtesy of Dr. John Jacoway.) **B**. OKC. (Courtesy of Dr. John Jacoway.) **C**. Histology of OKC. (Courtesy of Dr. John Jacoway.)

bridge and frontal bossing, milia (Chapter 23), potential for mental retardation, ovarian fibromas, and increased incidence of cleft lip and palate. Figure 20.13B illustrates the presence of OKC. Figure 20.13C illustrates the pitted areas of the palms, and Figure 20.12D depicts the soles of the feet. Criteria include composites of major and minor categories in order to diagnose the syndrome (Evans et al., 1993).

Primordial Cyst. The term "primordial cyst" is a synonym for OKC (Neville et al., 1995). In older literature, the two are identified as separate entities, but microscopic evaluation has found what was previously referred to as a primordial cyst to be an OKC.

The **primordial cyst** technically develops in place of the existing tooth or before any calcification of the tooth. The prime location for the primordial cyst is in the third molar region. Histologically, the primordial cyst is almost always diagnosed as an OKC. This type of cyst is usually painless and found on routine radiographic examination. The cysts are usually diagnosed in young adults and children.

NAME: Calcifying odontogenic cyst (Gorlin cyst)

Etiology: The World Health Organization, 2005, defined the **calcifing odontogenic cyst (COC)** as a benign cystic neoplasm of odontogenic tumor characterized by an ameloblastoma-like epithelium with ghost cells that may calcify and exhibit both radiolucent qualities along with some dispersed calcified material. The calcifying odontogenic cyst is believed to be derived from the reduced-enamel epithelium or odontogenic epithelium. Variations on the types of the COC with nonneoplastic, neoplastic, and malignant variations are still being debated (Sonawane et al., 2011), but for the purposes of this publication, the COC with other classifications are being treated as one. Both a cystic form and a solid neoplasm are recognized.

Method of Transmission: Not applicable

Epidemiology: The calcifying odontogenic cyst may occur at any age, but it is most often found in the second decade and usually in individuals under the age of 40. Jones et al.

FIGURE 20.13. **A**. Facial basal cell carcinoma. Large and small basal cell carcinomas are visible on the cheeks and chin. **B**. Odontogenic keratocyst in multiple areas with larger OKC in the left mandible. **C**. Plantar palmar pits in nevoid basal cell syndrome. **D**. Sole of foot exhibiting pitting. (All courtesy of Dr. John Jacoway.)

(2006) reported results from a patient population of 7,121 odontogenic cysts. The patient age groups for finding calcifying odontogenic cysts were 5 to 79 years, with an average age of 41.5. Jones et al. report the cysts occurring more often in males. Others (Regezi et al., 2003) report them occurring more often in females. Calcifying odontogenic cysts occur equally in the mandible and maxilla, with a propensity toward the anterior regions.

Pathogenesis: The calcifying odontogenic cyst (sometimes called the Gorlin cyst, as reported by Gorlin in 1962) is seen radiographically with varying amounts of radiodensity.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: Calcifying odontogenic cysts may be found as masses within the oral tissues, but this is rarely observed. When they do occur, they may resemble a gingival cyst or a peripheral giant cell fibroma. These cysts can occur in any location and present as an expansile intraosseous lesion or tender gingival swelling. Radiographically, the calcifying odontogenic cysts are unilocular or multilocular radiolucencies that exhibit clearly defined margins. Mixtures of calcifications and radiolucent properties are usually seen on the radiograph. Figure 20.14 depicts a radiograph of a calcifying odontogenic cyst.

Distinguishing Characteristics: The presence of "ghost cells" when the specimen is viewed microscopically is a diagnostic

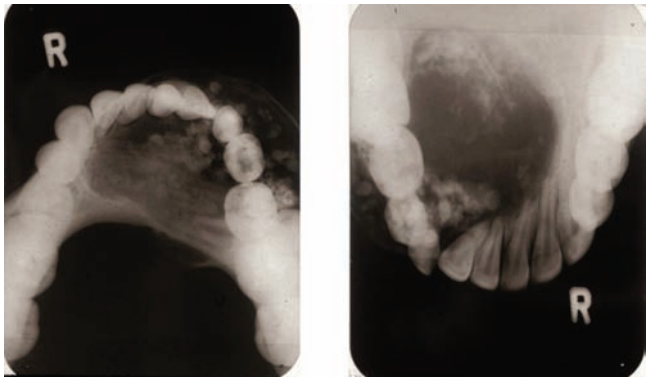


FIGURE 20.14. Calcifying odontogenic cyst. (Courtesy of Dr. Shabnum Meer.)

feature of the calcifying odontogenic cyst. These are epithelial cells that appear to have pink cytoplasma and have no nucleus. These are the cells which calcify. Root divergence is often observed.

Significant Microscopic Features: As mentioned above, a key feature of this type of cyst is the presence of ghost cells with dystrophic calcification. The ghost cells are composed of keratin with lost nucleus appearing more "clear" in form. These types of cells may be found in other odontogenic tumors also. Calcifications may be seen as well and may exhibit larger areas of opacities. The microscopic appearance may resemble that of the ameloblastoma in some cases. There is a neoplastic lesion resembling the ameloblastoma called epithelial odontogenic ghost cell tumor that is a more solid variant with very aggressive behavior.

Dental Implications: Definitive diagnosis is important to rule out more aggressive lesions, and complete removal is necessary.

Differential Diagnosis: The diagnosis depends upon microscopic examination, but to begin a differential diagnosis, the radiographic appearance is initially evaluated. The degree of the radiolucent and radiopaque qualities determines the order of the following differential diagnoses:

1. Dentigerous cyst, Chapter 20
2. Odontogenic keratocyst, Chapter 20
3. Ameloblastoma, Chapter 18
4. Adenomatoid odontogenic tumor, Chapter 20
5. Odontoma, Chapter 19

Treatment and Prognosis: Surgical excision is recommended for the cystic type of calcifying odontogenic cyst. The neoplastic type must be treated as an ameloblastoma with aggressive protocol. Correct pathological identification of the type of COC is crucial since these may vary and may be confused with other entities. The prognosis is good, although recurrence is sometimes seen.

NAME: Globulomaxillary cyst

Etiology: The **globulomaxillary cyst** was believed to represent a fissural cyst that arose from epithelium that was thought trapped when the globular portion of the median nasal process fused with the maxillary process, but has essentially been deemed by some oral pathologists as unlikely. It is thought that the majority represent multiple types of cysts such as a periapical or lateral periodontal cyst, laterally placed radicular cysts, central giant cell tumors, myxomas, and OKC, as well as others (Haring et al., 2006).

Method of Transmission: Not applicable

Epidemiology: Not applicable, since the cysts may be multiple variations and most are discussed within Chapter 20.

Pathogenesis: Globulomaxillary cyst is a vague term for a lesion in the globulomaxillary region between the maxillary lateral incisor and canine. The name globulomaxillary is linked to the location of the cyst. A biopsy is necessary to determine the diagnosis of the determined lesion and to classify the cyst.

Extraoral Characteristics: Extraoral characteristics do not occur unless the lesion is extremely large.

Perioral and Intraoral Characteristics: The cyst may be an inverted pear-shaped lesion because of the location, causing divergence of the tooth roots. It is circumscribed and radiolucent. Vitality of the pulp provides some evidence about the type of cyst.

A classic radiographic characteristic of the cyst is the divergence of the roots when the lesion is large enough to cause this factor. Figure 20.15 shows a globulomaxillary cyst in which root divergence is noted.

Distinguishing Characteristics: The location and the pear-shaped configuration of the globulomaxillary cyst give it a classic type of presentation. However, a biopsy is needed to determine the cyst type.

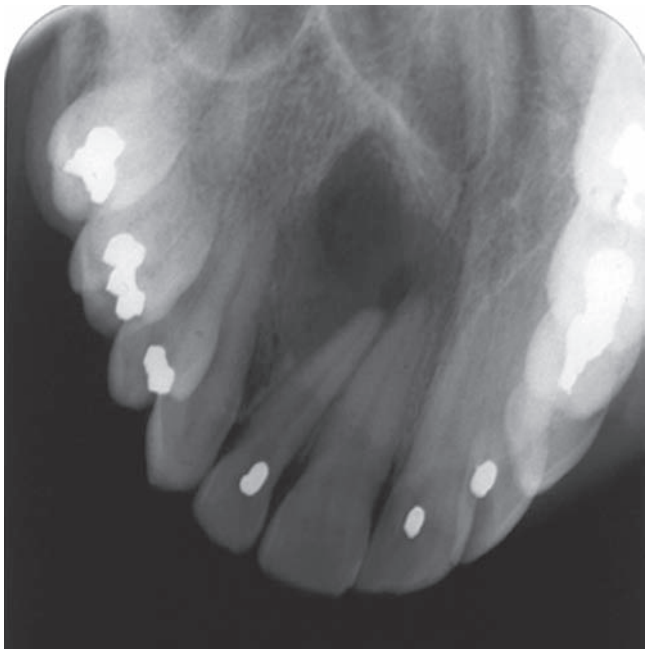


FIGURE 20.15. Globulomaxillary cyst. (Courtesy of Dr. Lynne Solomon.)

Significant Microscopic Features: The tissue sample provides evidence as to which type of cyst has occurred in this location. Again, the term "globulomaxillary" applies to location, with varying cysts occurring in an anatomic sense.

Dental Implications: The vitality of the teeth involved, such as the lateral and cuspid, must be evaluated. Endodontic therapy should be administered when necessary.

Differential Diagnosis: Considerations include many types of cysts including:

1. OKC, Chapter 20
2. Lateral periodontal cyst, Chapter 20

Treatment and Prognosis: Surgical removal is the treatment of choice, and the prognosis is good, depending upon the type of cyst. Recurrence is rare. Any resemblance to the OKC should be evaluated frequently because of the higher recurrence rate involved with these cysts. Treatment will depend upon the microscopic evaluation of the lesion.

NAME: Glandular odontogenic cyst

Etiology: The **glandular odontogenic cyst (GOC)** is derived from odontogenic origins. It is a locally aggressive odontogenic cyst.

Method of Transmission: Not applicable

Epidemiology: The GOC is considered rare, comprising only 0.2% of all odontogenic cysts. Over 100 cases have been reported in the English literature. There is no gender preference. In a study by Fowler et al. (2011), the mean age of 46 cases was 51 years, with 71% of cases in the fifth to seventh decades. Eighty percent of the cases occurred in the mandible with 60% occurring in the anterior region, but the canine region was noted for the occurrence when in the maxillary location. A high recurrence rate is reported within 5.8 years. The mean occurrence rate from initial treatment to first recurrence was 8 years and from first recurrence to second recurrence was 5.8 years.

Pathogenesis: Develops from odontogenic structures.

Extraoral Characteristics: Some clinical swelling/expansion has been noted as the common complaint.

Perioral and Intraoral Characteristics: Both swelling and expansion may be noted. Some cases are asymptomatic. Some reports of pain/discomfort, infection, and paresthesia have also been reported.

Distinguishing Characteristics: The most distinguishing characteristics are those that differentiate the GOC from other cyst structures. The mucoepidermoid carcinoma may be considered because of a shared histology with the GOC and with other entities such as the dentigerous cyst that may display some metaplastic changes.

Significant Microscopic/Radiographic Features: A well-defined unilocular or multilocular radiolucency involving the periapical area of multiple teeth (Fig. 20.16). Small duct-like spaces make the entity appear glandular on radiograph. Some lesions may display a scalloped border. Histologically, Fowler et al. (2011) state that some features appear to differentiate the GOC from other mimickers: microcysts, epithelial spheres, clear cells, variable thickness of the cyst lining, and multiple compartments are of value in differentiation. Eosinophilic cuboidal cells (hobnail cells) that are present on the surface of the cyst lining are a component for diagnosis.

FIGURE 20.16. Glandular odontogenic cyst. (Courtesy of Dr. Harvey Kessler)

Dental Implications: Follow-up is important since the recurrence rate is at least 50%. Radiographic examinations are important in an early diagnosis of recurrence.

Differential Diagnosis: The GOC may have characteristics similar to those of mucoepidermoid carcinoma, the dentigerous cyst, the radicular cyst, and surgical ciliated cyst.

Treatment and Prognosis: Most cases are treated conservatively with enucleation, curettage, cystectomy, and excision. There is a recurrence rate of 50%.

NAME: Nasopalatine canal cyst (incisive canal cyst, nasopalatine duct cyst)

Etiology: The **nasopalatine canal cyst** is considered a developmental cyst, located in the nasopalatine canal. This cyst arises from epithelial remnants of the embryologic structure of the nasopalatine ducts, and the structure connects the oral and nasal cavities in the area of the incisive canal, probably because of infection or some stimulation.

Method of Transmission: Not applicable

Epidemiology: It is the most common cyst that is not of odontogenic origin and occurs in about 1% of the population. The nasopalatine cyst is most commonly seen in the fourth to sixth decades, and there is a male predilection (Righini et al., 2004).

Pathogenesis: The nasopalatine cyst is also known as the incisive canal cyst, and when located in the incisive papilla, it is called cyst of palatine papilla. The cysts are developmental and are located within the nasopalatine canal proximity or the incisive papillae.

Extraoral Characteristics: The size and extent of the cyst determine any extraoral characteristics such as swelling and elevation of the external surfaces around the nose and lip areas.

Perioral and Intraoral Characteristics: The patient may complain of pain, tenderness, and swelling, and drainage may be noted in the maxillary incisor region. When the lesion develops in the soft tissues of the incisive papillae, it is referred to as a cyst of the incisive canal. Usually, the lesion has a dark-red to bluish hue in this region.

Radiographically, the nasopalatine cyst is seen between the maxillary central incisors. The lesion is a well-circumscribed radiolucent lesion, which may have a sclerotic border. Figure 20.17A illustrates a nasopalatine cyst above the maxillary central incisors.

Distinguishing Characteristics: When drainage occurs with the nasopalatine cyst, the patient may complain of a foul, salty taste. The patient may also experience pain, discomfort, and burning.

Significant Microscopic Features: The lining of the cyst is composed of stratified squamous epithelium (most common), pseudostratified columnar epithelium, simple columnar epithelium, or simple cuboidal epithelium. Nerves and small vessels may be found in the connective tissue wall. Figure 20.17B depicts the histology of a nasopalatine cyst containing a flattened cuboidal epithelial lining.

Dental Implications: The cyst is not radiographically diagnostic and must be removed and biopsied for definitive microscopic evaluation.

Differential Diagnosis: Other cysts may be considered such as:

1. Radicular cyst, Chapter 20
2. Periapical granulomas, Chapter 20
3. Median palatine cyst, Chapter 20

Treatment and Prognosis: Complete surgical removal is needed. The prognosis is good, and the recurrence rate is low with complete removal. There is a tendency to overdiagnose these lesions since radiographic shadows occur in this region due to the anatomy.

Median Palatine Cyst. The median palatine cyst (MPC) is located in the same vicinity as the nasopalatine cyst but is more apically centered toward the midline of the hard palate. The lesion is lined by stratified squamous epithelium and is surrounded by dense connective tissue. The MPC is classified as a rare fissural cyst and is believed to develop from entrapped epithelium along the embryonic line of fusion in the two lateral maxillary processes that fuse to make the hard palate. There is controversy around this entity. The World Health Organization, in 1992, questioned the validity of the MPC and proposed the fact that other cysts are much more likely, such as the nasopalatine duct cyst or keratocyst, depending upon the location. Queiroz et al. (2011) raised the issue that it may be difficult to differentiate the nasopalatine cyst from the MPC. The patient may complain of pain and expansion of the palate when the cyst impinges the nasopalatine nerve. There is a reported male predilection of 4:1 with an age range of 13 to 52 years. Bacci et al. (2011) also raised the issue of criteria needed to make a diagnosis of MPC. Pathologists are still debating the diagnostic confirmation criterion of the MPC.

Figure 20.18 depicts a median palatine cyst.

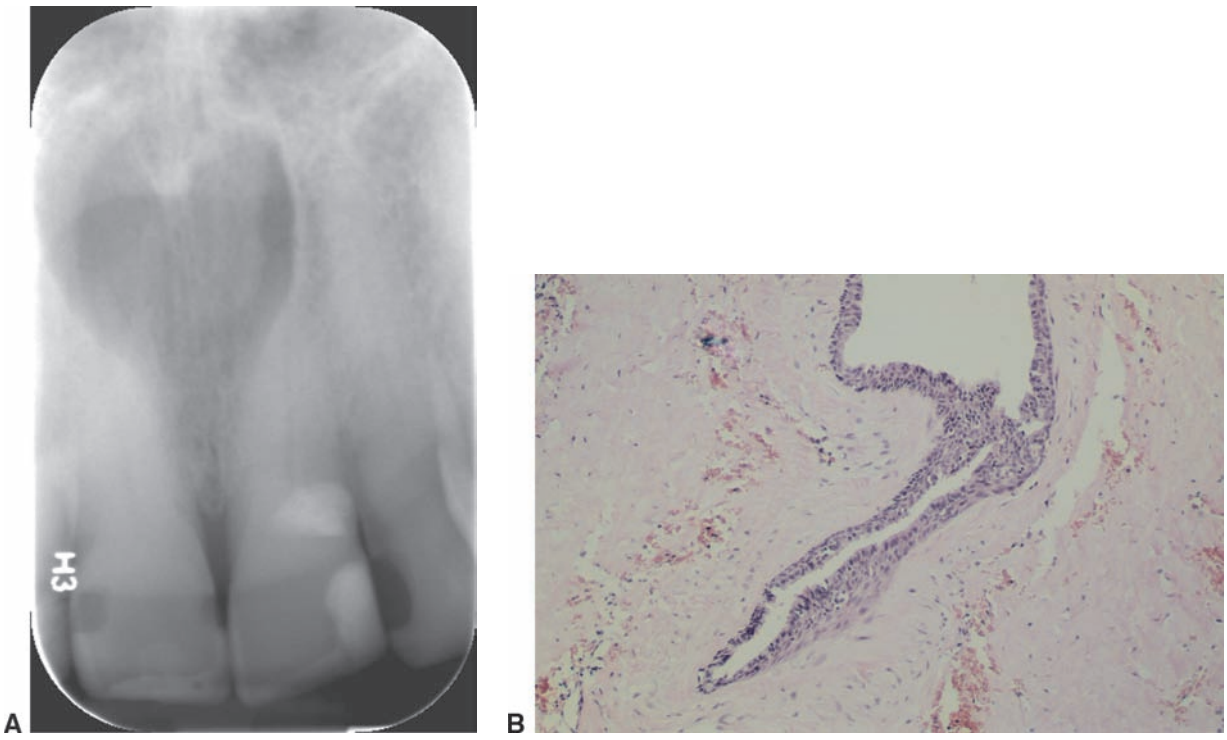


FIGURE 20.17. **A**. Nasopalatine duct cyst. (Courtesy Dr. Harvey Kessler) **B**. Histology of the nasopalatine duct cyst. (Courtesy of Dr. John Jacoway.)

FIGURE 20.18. Median palatine cyst. (Courtesy of Dr. John Jacoway.)

FIGURE 20.19. Static bone cyst. (Courtesy of Dr. Shabnum Meer.)

NAME: Static bone cyst (Stafne bone defect, static defect)

Etiology: The **static bone cyst** is not a true cyst, although by all appearances on a radiograph, it resembles a cyst. Technically, the static bone cyst is a defect in the mandible that surrounds salivary gland tissue. It is believed to be entrapment of the salivary gland tissue and is not lined by epithelium.

Method of Transmission: Not applicable

Epidemiology: The static bone cyst is seen in adults, and most static bone cysts are unilateral and believed to be present from birth. Studies have reported cases involving children as well, although few cases are reported in the literature (Campos et al., 2004).

Pathogenesis: It is believed that the static bone cyst results from lingual mandibular cortical bone erosion from hyperplastic salivary gland tissue or entrapment of salivary gland tissue during the development of the mandible.

Extraoral Characteristics: Not applicable

Perioral and Intraoral Characteristics: The static bone cyst is asymptomatic and is usually discovered when a Panorex film is taken. On a radiograph, the bone cyst is seen as radiolucency in the posterior mandible below the mandibular canal. The static bone cyst is a sharply circumscribed, oval, radiolucent lesion with a sclerotic border.

Distinguishing Characteristics: The static bone cyst is usually found at the angle of the mandible (Fig. 20.19).

Significant Microscopic Features: The static bone cyst is a defect, which, if biopsied, may contain submandibular gland tissue, some blood vessel, muscle, and fat.

Dental Implications: The static bone cyst is usually diagnosed clinically by using radiographs; however, when the location is superior to the mandibular canal, a biopsy may be needed to rule out pathology.

Differential Diagnosis: The location and the appearance of the lesion is confirmation in most cases. Radiographs are followed long-term for any changes.

Treatment and Progress: The static bone cyst is noted and followed long-term and if any changes occur, they are noted in the patient's record. Other cysts should be considered if the cyst is occurring above the mandibular canal.

Neoplasms

As discussed in previous chapters, a neoplasm exhibits uncontrolled growth. This chapter discusses neoplasms that have a radiolucent appearance when viewed on a radiograph. The neoplasms discussed in this section are the adenomatoid odontogenic tumor (AOT), the odontogenic myxoma, the ameloblastic fibroma, and Langerhans cell disease. All of these neoplasms exhibit growth potential, and they each appear radiolucent on radiographs. Certain neoplasms may originate from metastatic cancer as well and will also appear radiolucent. This type of neoplasm is discussed in Chapter 5.

NAME: Adenomatoid odontogenic tumor

Etiology: Once thought to be a variant of the ameloblastoma, the **adenomatoid odontogenic tumor** (AOT) is now classified as an encapsulated benign epithelial odontogenic tumor.

Method of Transmission: Not applicable

Epidemiology: The AOT is usually seen between the ages of 5 and 30 years. Most patients are under 20 years of age. There is a female predilection of 2:1, and some experts report an even larger percentage of females with the tumor (Ajinkya et al., 2011). The anterior maxilla is the favored location. AOTs are found associated with impacted teeth (Batra et al., 2005; Varkhede et al., 2011). Although the maxillary canines are often affected, other areas may be involved as well, such as the mandibular region and the molar region (Anegundi et al., 2011; Bhullar et al., 2011). The tumors affect approximately 2 to 7% of all odontogenic tumors. Various forms of the tumor may exist but usually this tumor is seen as a unilocular radiolucency around the crown of an unerupted tooth. Seen less often is the form located between the roots of several erupted teeth. Three variations are associated with the AOT: follicular, extrafollicular, and peripheral (Sharma et al., 2012).

Pathogenesis: The AOT is a benign epithelial tumor with a dense fibrous connective tissue capsule, which usually does not recur once adequately removed. It is a benign tumor and commonly appears in the anterior portion of the maxilla.

Extraoral Characteristics: Swelling in the facial area is sometimes reported, causing flaring of the nasolabial fold and extending beyond the facial contour.

Perioral and Intraoral Characteristics: As the tumor expands and increases in size, there may be root displacement and a bony hard expansion with an eggshell cracking appearance over the protrusion.

For the most part, this tumor appears radiolucent on radiograph but may exhibit small opaque foci within the tumor. The number and size of the foci determine the radiographic appearance of the lesion. Figure 20.20A shows the radiographic view of an AOT. Figure 20.20B depicts the intraoral AOT.

Distinguishing Characteristics: The microscopic features of this tumor are distinguishing characteristics. The glandular or duct-like features forming a rosette pattern clearly differentiates the AOT from others lesions through histology (Robledo & Mazock, 2011).

Significant Microscopic Features: As mentioned above, the rosettes and duct-like features are very characteristic of this tumor. These patterns are composed of duct-like structures of columnar epithelial cells and consist of polyhedral spindle cells organized in sheets and lobules. The nuclei of the cells are polarized away from the central spaces. Figure 20.20C depicts the histology of the oral AOT, demonstrating the rosette pattern.

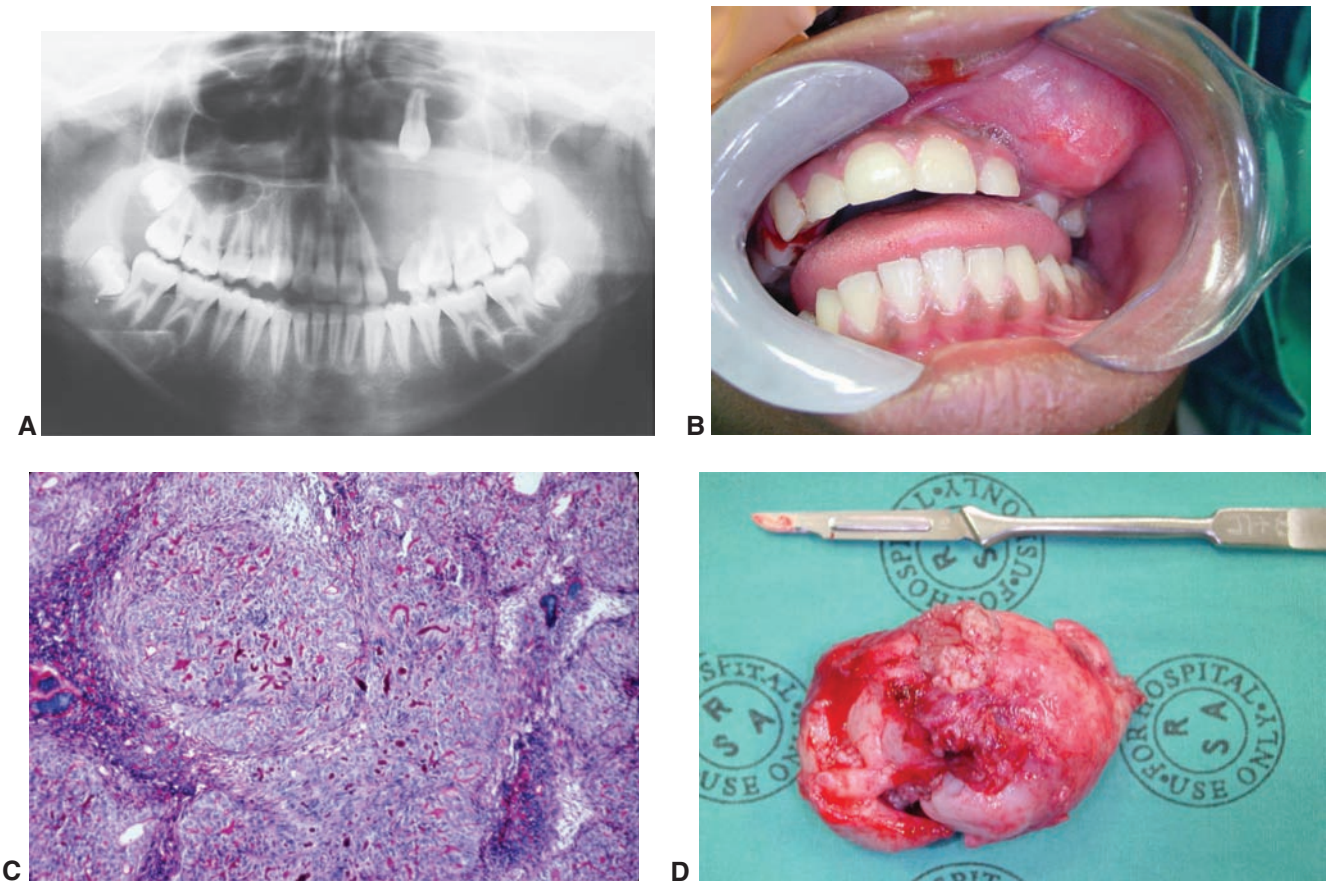


FIGURE 20.20. Adenomatoid odontogenic tumor. **A**. Note the retained and displaced cuspid due to the large growth of the tumor. (Courtesy of Dr. Shabnum Meer). **B**. The tumor fills the labial space above tooth 11 and tooth 12. (Courtesy of Dr. Shabnum Meer). **C**. The classic rosette pattern is depicted. (Courtesy of Dr. James Sciubba.) **D**. Surgically removed AOT. (Courtesy of Dr. Shabnum Meer).

Dental Implications: Facial asymmetry is one of the first signs to be noticed by the patient as the tumor increases in size. The tumor expands and should be excised. Figure 20.20D depicts a large AOT after removal of the lesion depicted in the previous images.

Differential Diagnosis: Considerations include:

1. Dentigerous cyst because of the occurrence around impacted teeth, Chapter 20
2. Calcifying epithelial odontogenic tumor when calcifications are present, Chapter 18
3. Ameloblastoma, Chapter 18
4. Odontogenic keratocyst, Chapter 20

Treatment and Prognosis: Complete removal of the tumor is necessary, and the prognosis is excellent without any recurrence.

NAME: Odontogenic myxoma

Etiology: The **odontogenic myxoma** is derived from odontogenic ectomesenchyme, and it originates in the PDL or dental pulp.

Method of Transmission: Not applicable

Epidemiology: Odontogenic myxoma usually occurs in the 10- to 30-year-old age group. It is rare in the over 50-year-old age group. There is no gender preference for this lesion (Ogutcen-Toller et al., 2006). Myxomas are seen equally in the maxilla and the mandible.

Pathogenesis: Myxomas are benign neoplasms that are capable of rapid growth and are very persistent. Root resorption and displacement may be seen in some cases. This is not an encapsulated tumor.

Extraoral Characteristics: Depending upon the size of the myxoma, swelling may occur in isolated areas.

Perioral and Intraoral Characteristics: Radiographically, the tumors can be unilocular or multilocular, and the radiolucencies may have a scalloped appearance. Myxomas have also been described as having a "step ladder" or "honeycombed" appearance. The margins may be well defined or they may be diffuse. Figure 20.21 illustrates a myxoma in the lower right molar region. Note the soap bubble appearance around the molar and bicuspid regions.

Distinguishing Characteristics: Not applicable

Significant Microscopic Features: The features are stellate-shaped cells and fine collagen fibrils. The specimen is gelatinous and pulp-like.

Dental Implications: Enlarged dental follicles or the dental papilla of a developing tooth may be mistaken for the myxomas upon microscopic examination. They also can be confused with other myxoid jaw neoplasms. The tumors can become quite large, causing tooth displacement.

Differential Diagnosis: Considerations include:

1. Odontogenic fibroma, Chapter 17
2. Ameloblastoma, Chapter 18
3. Hemangiomas of bone, Chapter 20

Treatment and Prognosis: The myxoma is removed surgically with chemical cautery. The highly gelatinous material makes removal difficult, and the recurrence rate is as high as 25% because the tumor is nonencapsulated. Fragments are difficult to remove.

NAME: Ameloblastic fibroma (fibro-odontoma)

Etiology: The **ameloblastic fibroma** is a mixed odontogenic tumor that is believed to originate from odontogenic ectomesenchyme and odontogenic epithelium.

Method of Transmission: Not applicable

Epidemiology: Ameloblastic fibromas are seen infrequently. They are usually slow growing and small in size, although large tumors have been reported. A study by Buchner (1991) reported the relative frequency of central odontogenic tumors in relation to all biopsy specimens submitted to a biopsy service. After excluding the odontomas, which accounted for

FIGURE 20.21. Odontogenic myxoma. (Courtesy of Dr. Enrique Platin.)

75.9% of all odontogenic tumors, the ameloblastic fibromas (accounting for 6.5%) were seen less frequently than ameloblastomas (48.5%), myxomas (9.2%), and AOTs (7.3%). The lesions are usually seen early in life before the age of 20, but some have been reported in the third and fourth decades. The posterior mandible is the most common site. There is no gender preference. Recent studies by Jindal and Bhola (2011) raise the issue of whether the ameloblastic fibromas are hamartomas or a true neoplasm. Depending upon the composition of the tumor, other classifications are used such as the ameloblastic fibro-odontoma (if dentin and enamel are present) or ameloblastic fibrodentinoma (if only dentin is present) (Costa et al., 2011). As more information and documentation is gained about many of the entities in this chapter, modifications are made and terms may be changed.

Pathogenesis: The lesions are composed of neoplastic epithelium and neoplastic myxomatous connective tissue and are usually associated with third molars (Regezi, 2003).

Extraoral Characteristics: Depending upon the expansion, some external swelling may be present.

Perioral and Intraoral Characteristics: The patient usually experiences no pain with any swelling that may occur. The ameloblastic fibroma has potential for extensive growth causing jaw expansion. Occasionally, there may be calcified material containing enamel and dentin. If so, the lesion is identified as an ameloblastic fibro-odontoma.

Radiographically, the lesion can be unilocular or multilocular. It is normally well defined and usually associated with an unerupted tooth. Figure 20.22 illustrates the ameloblastic fibroma seen in the molar region as a well-circumscribed lesion with a sclerotic border.

Distinguishing Characteristics: The histology of the ameloblastic fibroma is unusual and highly diagnostic (see below for details).

Significant Microscopic Features: The ameloblastic fibroma is composed of long strands and islands of odontogenic epithelium set in an immature cellular matrix resembling the dental papilla (mesenchymal component) or developing dental pulp. The strands are usually only two cells thick of cuboidal or tall columnar cells. The stroma sets it apart from the ameloblastoma. The ameloblastic fibroma presents as a pulp-like stroma with islands of ameloblastic epithelium. The tall columnar cells resemble ameloblasts around stellate reticulum.

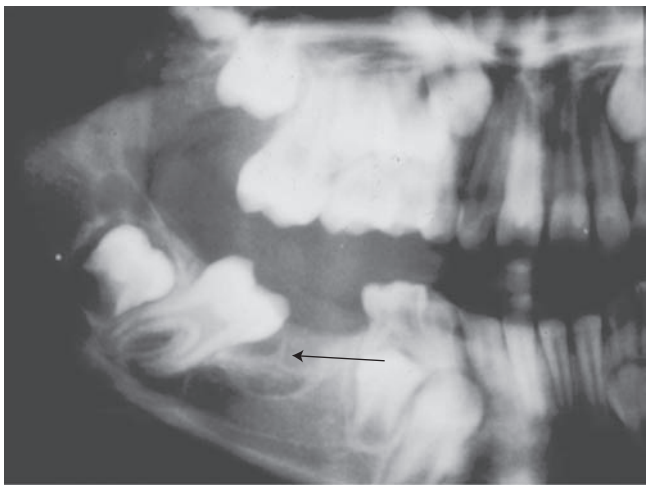


FIGURE 20.22. Radiograph of ameloblastic fibroma. (Courtesy of Dr. Harvey Kessler.)

Dental Implications: Generally, the ameloblastic fibroma is asymptomatic.

Differential Diagnosis: Other entities are considered when the lesion appears to deviate from normal radiologic patterns, and the size of the lesion or age of the patient may be out of the usual range. The ameloblastic fibroma may appear as the early stages of the following:

1. Ameloblastoma, Chapter 18
2. Odontogenic myxoma, Chapter 20
3. Dentigerous cyst, Chapter 20
4. Odontoma, Chapter 19
5. Dentigerous cyst, Chapter 20
6. Myxoma, Chapter 20
7. Odontogenic keratocyst, Chapter 20
8. Central giant cell granuloma, Chapter 18

Treatment and Prognosis: Conservative excision is the treatment of choice. Recurrence is seen in approximately 20% of cases. Some recurrences of ameloblastic fibrosarcomas have been reported in previously benign cases of ameloblastic fibromas.

NAME: Langerhans cell disease

Etiology: The basic cause of **Langerhans cell disease**, formally called histocytosis X, is unknown. It involves proliferation of the Langerhans cells, which normally reside in the epidermis and mucosa. The other cells involved are the histocytes and eosinophils; specifically identified are Birbeck granules and a few macrophages. In some cases, a neoplastic transformation is believed responsible for this disease. An immune response has also been implicated. Additionally, a neoplastic process and a reactive process have been suggested as causal.

Method of Transmission: Not applicable

Epidemiology: Langerhans cell disease usually involves young adults and children. Over 50% are under the age of 10. However, the age range can extend to older adults. Males are affected more than females (Buchmann et al., 2006).

Pathogenesis: Three distinct disorders are involved in the disease and recognized as variants of the disease (Lieberman et al., 1996; Muramatsu et al., 2010). They include:

1. Eosinophilic granuloma—This disorder occurs in young adults or adults. Bone lesions are present and exhibit as well-defined radiolucent lesions. When found in the mouth, the posterior mandible is most often affected, which results in displaced teeth and fractures

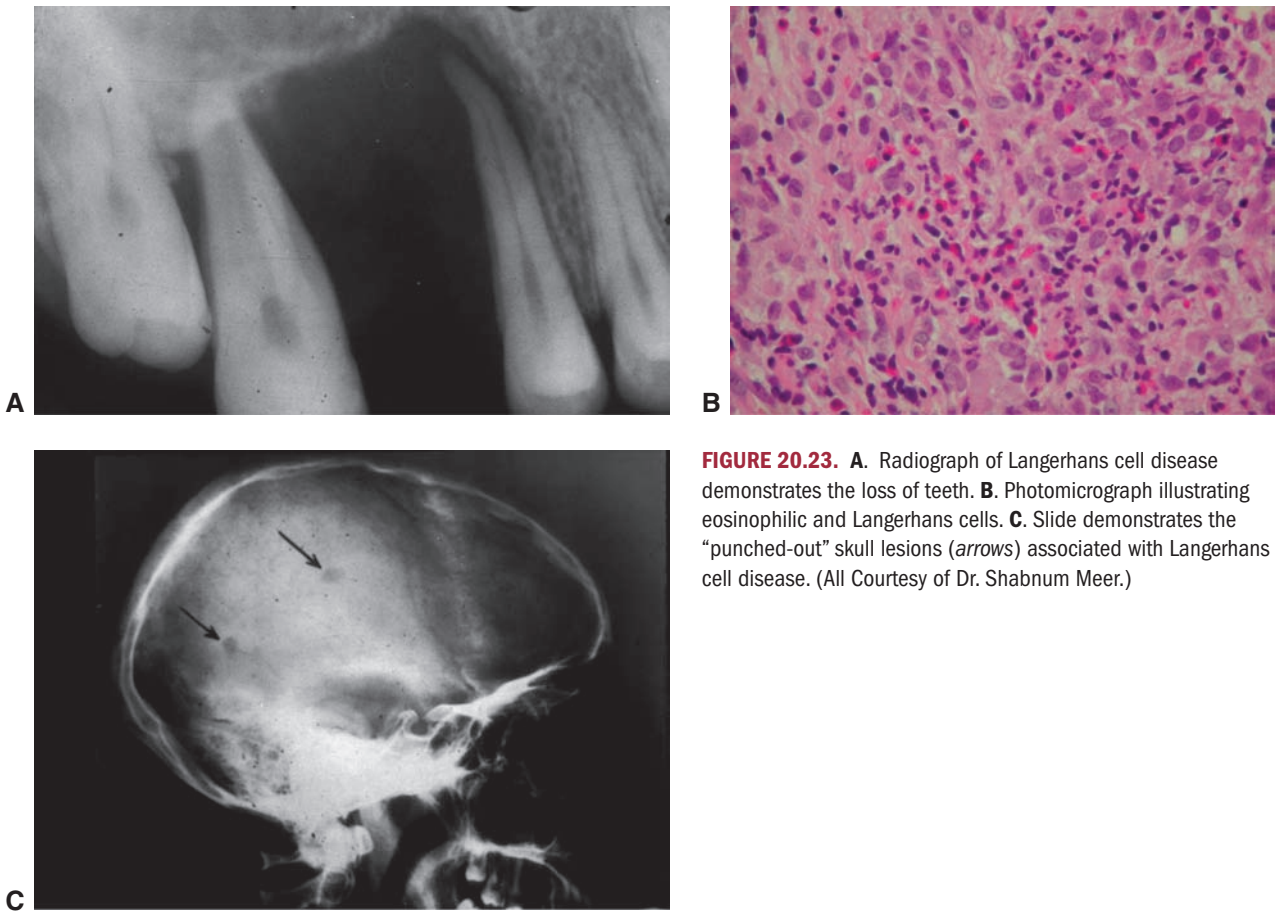


FIGURE 20.23. A. Radiograph of Langerhans cell disease demonstrates the loss of teeth. **B**. Photomicrograph illustrating eosinophilic and Langerhans cells. **C**. Slide demonstrates the "punched-out" skull lesions (*arrows*) associated with Langerhans cell disease. (All Courtesy of Dr. Shabnum Meer.)

(described as floating teeth). Oral ulcerations are usually present. Figure 20.23A illustrates a radiograph that exhibits floating teeth and bone destruction. Figure 20.23B is a photomicrograph illustrating eosinophilic granuloma in Langerhans cell disease.

2. Hand-Schüller-Christian disease—This variant is termed multifocal eosinophilic granuloma. This disorder primarily affects children, usually under 5 years old, and results in diabetes insipidus, punched out lesions, and ophthalmus. Skin lesions may or may not be present. The patient may have persistent oral lesions including gingival ulcerations. Halitosis and difficulty healing are also characteristic. Skull lesions exhibit a "punched-out" appearance (Fig. 20.23C) (Mortellaro et al., 2006).
3. Letterer-Siwe disease—Infants are especially affected by this disease. A rash may be the first sign of the disorder. Ear infections, lymphadenopathy, fever, anemia, and other infections are all known to occur. Bone lesions may or may not be seen radiographically. The disease has been associated with a lymphoma. The course of the disease is extremely rapid, with a poor prognosis.

Extraoral Characteristics: Poor healing is common with Langerhans cell disease, dermatologic conditions may be evident, and all bones of the body may be affected. Lymphadenopathy may be present, cranial bones may be involved, and the cutaneous areas may involve rashes and erythematic lesions. Radiographically, the bone lesions resemble a "punched out" appearance with sharply demarcated lesions.

Perioral and Intraoral Characteristics: The disease may involve one or more multiple bones in the body, including the bones around the teeth, contributing to loosening (called "floating teeth"). Tenderness, pain, and swelling are common complaints. The patients may overlap in the above stated symptoms and may or may not exhibit the stated characteristic symptoms, depending upon the stage and type of the disorder.

Distinguishing Characteristics: A key characteristic of Langerhans cell disease is premature loosening and exfoliation of teeth in children.

Significant Microscopic Features: The microscopic features involve large histiocytoid cells mixed with eosinophils. Birbeck granules within the Langerhans cells are diagnostic factors. These cells have large abundant cytoplasm and are arranged in sheets.

Dental Implications: Lesions that occur periapically can be confused with periapical cyst or granulomas. Tooth vitality would still be present.

Differential Diagnosis: Some considerations are:

1. Juvenile periodontitis
2. Leukemia, Chapter 9

3. Malignant neoplasms, discussed throughout the book
4. Multiple myeloma, considered when well-circumscribed radiolucencies are present

Treatment and Prognosis: The treatment depends upon the involvement of the disease and the age of the patient. Conservative surgical treatment is sometimes the only treatment. However, in more extensive disease involvement, chemotherapy may be needed as well. Additionally, bone marrow transplantation may be done; but essentially, the more widespread the lesions, the poorer the prognosis. The prognosis is more favorable when the disease states develop in older young adults.

SUMMARY

- Cysts are fluid-filled cavities lined with epithelium.
- Odontogenic cysts are cysts with an epithelial lining that is formed from the remnants of the tooth-forming organ: the rests of Malassez (rests of the root sheath of Hertwig), glands of Serres (rests of the dental lamina), and reduced enamel epithelium (remnants of the enamel organ).
- The periapical granuloma or dental granuloma (also called apical periodontitis) is the result of necrotic pulp tissue and by-products resulting from an inflammatory process that has damaged the tissue at the apex of the tooth.
- The radicular cyst is always associated with a nonvital tooth, and the common causes are caries, trauma, or periodontal disease. The cyst is epithelial lined. They occur due to stimulation of the rests that have lain dormant until activated.
- Three variants of cementoosseous dysplasia are periapical COD (formerly called cementoma), focal COD, and florid COD.
- A periapical abscess is most often the cause of the acute form of osteomyelitis.
- The traumatic bone cyst (also called the simple bone cyst) is thought to be caused by trauma. This cyst is not considered a true cyst because it is not epithelium lined.
- Lateral periodontal cysts are odontogenic, nonkeratinized developmental cysts and are believed to develop from the dental lamina remnants (rests of Malassez) from within bone. A variant of lateral periodontal cysts are multilocular cysts that are termed botryoid odontogenic cysts.
- Dentigerous cysts are odontogenic in development and arise from a cystic change in the dental follicle after crown formation. They are associated with the crown of an unerupted tooth.
- The paradental cyst is derived from the enamel epithelium and is thought to be a variant of the dentigerous cyst.
- The primordial cyst develops at a site where a tooth fails to develop. These are thought to be keratocysts on histological evaluation.
- The eruption cyst is considered a variant of the dentigerous cyst and is caused by the accumulation of fluid or blood between the crown of an erupting tooth and the reduced enamel organ, caused by trauma.
- The aneurysmal bone cyst is considered a pseudocyst in that it appears as a cyst, but unlike the true cyst, does not have an epithelium-lined lumen. This cyst is blood filled, expansile, and increases risk of fracture.
- Gingival cyst of the newborn occurs on the ridges of the oral tissues in the newborn. The nodules are multiple small cysts found at the junction of the hard and soft palates and along buccal and lingual dental ridges.
- The odontogenic keratocyst (OKC) is developed from the dental lamina or its remnants. This cyst is aggressive and recurs because of many daughter cells in the tissue. It may be unilocular or multilocular.
- Nevoid basal cell carcinoma (BCC) syndrome, also known as Gorlin-Goltz syndrome, is of prime concern, since the OKC is associated with this syndrome. Patients have multiple jaw cysts and BCC in many areas. Palms of the hands and soles of the feet have pitting.
- Calcifying odontogenic cyst is believed to be derived from the reduced enamel epithelium or dental lamina remnants. Ghost cells are apparent in histology. There is a high recurrence rate.
- The nasopalatine canal cyst is a developmental cyst located in the nasopalatine canal. This cyst arises from epithelial remnants of the embryologic structure of the nasopalatine ducts, probably caused by infection or stimulation. Facial swelling is observed as cyst enlarges.
- The globulomaxillary cyst is believed to be odontogenic in origin and may represent a periapical or lateral periodontal cyst. Some believe that it is not a true entity but representative of other types of cysts.
- The glandular odontogenic cyst (GOC) has some microscopic similarities to the dentigerous cyst, a botryoid cyst, and the radicular cyst. They may be confused with some characteristics of a mucoepidermoid carcinoma (diagnosis through histology biopsy is crucial). Most occur in the mandible at the fifth decade. They involve the periapical of multiple teeth and have a scalloped appearance.
- The static bone cyst is a defect in the mandible that surrounds salivary gland tissue. It is believed to be entrapment of the salivary gland tissue and is not lined by epithelium.
- The adenomatoid odontogenic tumor (AOT) is classified as an encapsulated benign epithelial odontogenic tumor. Average age is 20 years old with a female predilection. Expansion, swelling, and an eggshell layer of bone are characteristic as the tumor grows.
- The odontogenic myxoma is derived from odontogenic ectomesenchyme and originates in the periodontal ligament (PDL) or dental pulp. It is nonencapsulated, persistent, and capable of rapid growth.
- The ameloblastic fibroma is a mixed odontogenic tumor that is believed to originate from odontogenic ectomesenchyme and odontogenic epithelium. It is associated with unerupted teeth, is usually seen before age 20, and may cause jaw expansion.
- Langerhans cell disease has three distinct subgroups: eosinophilic granuloma, Hand-Schüller-Christian syndrome, and Letterer-Siwe disease.

CHAPTER REVIEW

Case Study 20.1

Figure 20.24 is of a 73-year-old male who was on holiday from Germany visiting his daughter in the United States. He is a healthy male with no apparent health problems and is taking no medications. After a 10-hour flight and arrival in the United States, he began to have severe pain in the tooth 5 area. His daughter became concerned when the pain did not subside and brought him in to see the dentist. The patient did not speak English, and his daughter served as an interpreter. Clinically, the apical area on the gingiva was raised, erythematic, fluctuant, and painful when pressure was applied. There was no mobility. On the radiograph there is an obvious radiolucent lesion above the apices of tooth 5.

1. What would be your opinion of the lesion?
2. What do you think has caused the radiolucent lesion?
3. What do you believe would relieve the pain and pressure of the lesion?
4. Are there factors that may have contributed to the sudden appearance of this lesion?

For answers and additional review activities, log in to **thePoint.lww.com**

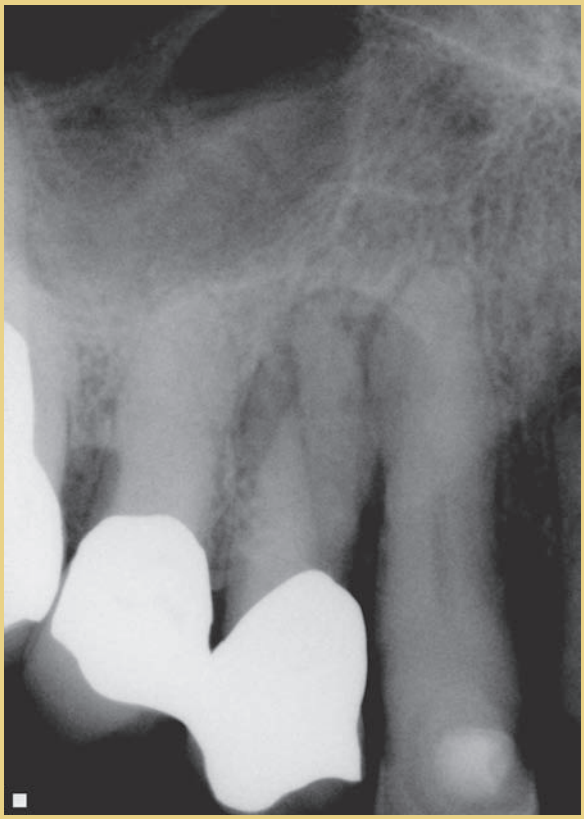


FIGURE 20.24. Courtesy of Dr. Kathryn Savitsky.

Case Study 20.2

Examine Figure 20.25 and answer the following questions.

1. What would be your estimation of the age of this patient?
2. What pathology may exist in this radiograph?
3. Do you think that any treatment or biopsy would be necessary?
4. Using the clinical protocols listed in the book, what helpful information would you be able to provide to the patient?

For answers and additional review activities, log in to **thePoint.lww.com**

FIGURE 20.25. Courtesy of Dr. Kathryn Savitsky and Jessica Huffman, RDH, MDH.

Critical Thinking Activities

Please study the image provided in Figure 20.12B (see p. 531). Study the object in the middle right side of the slide.

1. Does the small white area have anything to do with the odontogenic keratocyst in the ramus?
2. Is it in the spinal column?
3. What purpose does it serve?
4. Why does it appear as a white object?
5. Would it cause damage to the tissues?
6. Should the person have this removed?

Portfolio Possibilities

- Design a chart with the most commonly seen types of cysts, using radiographs and diagrams for patients to understand the locations where these cysts occur and how they differ in a differential diagnosis from other common cysts. This chart gives the patient a sense of how the clinician arrives at the diagnosis. The radiographs could be enlarged for easier viewing. The images could be placed in a slide presentation or keynote format and shown on your laptop or placed on the desktop of your clinic computer for easy access.
- Develop patient instructions for each commonly seen cyst. The material could provide information that is specific to each cyst and contain your office logo or referral information. Be sure to utilize the clinical protocols for individual patient needs. These could easily be printed out when linked to the specific cyst on your computer as well.

Media Menu

Web Sites

American Cancer Society
http://www.cancer.org/

American Dental Association
http://ada.org/

National Institutes of Health, Health Information
http://health.nih.gov/

Osteonecrosis and Bisphosphonates
http://www.sciencedirect.com/science/article/pii/s0306987711005834

Study Tools

Take advantage of additional online resources to help you study and ace your exams!

- Answers to case studies in the book
- Additional case studies and answers
- Interactive quiz bank with answer feedback
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- Expanded Media Menu with direct links to related Web sites and multimedia resources
- Supplemental references

thePoint Online resources and links are available at http://thepoint.lww.com/DeLong2e.

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Chapter 20 **LESION/CONDITION SUMMARY TABLE**

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Periapical granuloma	Caused by trauma, caries, and necrotic pulp damage	Chronically inflamed granulation tissue accumulates in the apical area of tooth.	Pain and sensitivity are reported. Tooth will test as nonvital.	Inflamed granulation tissue. Lymphocytic infiltrate of plasma cells, neutrophils, histiocytes and eosinophils. No epithelial lining.	Endodontics	Routine follow-up
Radicular cyst	Occurs in a nonvital tooth. Initially caused by periodontal disease, caries, fractures, or trauma. The inflammation begins stimulation of the rests.	Stimulation of epithelial rests. Most commonly occurring cysts of the jaws.	Pain in most cases; however, many are discovered on radiographic examination without any complaints reported by the patient.	Unlike the periapical granuloma, radicular cysts have an epithelial lining of nonkeratinized-stratified squamous epithelium.	Root canal therapy, and sometimes surgical extraction.	Close watch since incomplete removal of all diseased tissue may result in recurrence. This may result in a residual cyst. Pulp tests are necessary.
Aneurysmal bone cyst	Considered a pseudocyst since it does not have the epithelial lining of a true cyst	It is blood filled. May have a genetic component and may result from prior trauma.	Swelling with or without pain.	Multilocular lesion with a "soap bubble" appearance. No epithelial lining but is composed of immature connective issue with scattered multinucleated giant cells.	Excision and curettage. Improper removal may cause recurrence. A high recurrence rate is reported so complete enucleation is needed.	The teeth may become loose or displaced due to the bone expansion.
Traumatic bone cyst (simple bone cyst)	Prior trauma is implicated but other factors may be involved, such as calcium deficiency.	The bone does not heal from the trauma, liquefies and becomes a cyst (without an epithelial lining, i.e., a pseudocyst).	May cause swelling if large enough. Pain is usually not a factor.	Bone and blood products are seen without any evidence of epithelial content. The cyst is also seen radiographically as scalloping between the teeth. Margins may be very sharp.	Lesion is drained so that area can begin to heal. The bone will repair itself over time.	When these lesions are not detected early, they continue to expand. Radiographic follow-up is needed.
Cementoosseous dysplasia (COD) (cementoma)	Unknown reactive-type lesion	It is considered a reactive type lesion and some speculate that it may be related to a defect in the bone with remodeling of bone and cementum difficulty.	The patient is usually asymptomatic. Lesions usually discovered with a radiograph. Preference for the mandibular anterior region.	Fibrous connective tissue that can be seen with bone and cementum in varying stages of formation.	The tooth will test vital. Only observation is suggested.	No root canal will be needed—only observation. Early recognition is crucial to avoid unnecessary tests or surgery.
Focal cemento-osseous dysplasia	Unknown reactive-type lesion	Variant of COD	Asymptomatic and occurs most often in the posterior mandible region.	Fibrous connective tissue that can be seen with bone and cementum in varying stages of formation.	The tooth will test vital. Only monitoring will be needed.	No root canal will be needed—only observation.
Florid cemento-osseous dysplasia	Unknown reactive-type lesion. Affects blacks, Asians, and whites.	Variant of COD	Generally asymptomatic but may produce pain or pressure with secondary infections.	A yellow, granular bone-like material is present clinically and presents as a "ground glass" appearance on a radiograph.	Osteomyelitis may be a complication in severe cases.	Must be differentiated from Paget disease, chronic diffuse osteomyelitis, and Gardner syndrome.
Osteomyelitis	Bacteria enters the bone through an abscess, fracture, extraction site, etc.	Destruction of the bone occurs when bacteria enter the site. The osteomyelitis can reach a chronic form when the acute form is not resolved.	Fever with pain and lymphadenopathy	Specimen shows loss of osteocytes from lacunae and bacteria is present within the lesion.	Antibiotic coverage, drainage and surgery. Depending upon the type of bacteria and the form of the osteomyelitis.	Good once the infection is controlled.
Lateral periodontal cyst (botryoid odontogenic cyst)	Stimulation of epithelial rests.	Derived from dental lamina remnants within the bone. Usually in mandibular cuspid region and premolar region on the lateral surface.	Tooth is vital. When multilocular it is called botryoid odontogenic cyst.	Specimen will depict cuboidal epithelium lining within cyst. Clusters and whorls of cells with clear cytoplasm. Must rule out other types of cysts such as odontogenic keratocyst.	Surgical excision and microscopic evaluation.	Excellent prognosis with complete excision. Radiographic follow-up is needed.

Chapter 20 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Gingival cyst of the adult	Counterpart to the lateral periodontal cyst	Developmental and derived from the dental lamina, probably the rests of Serres.	Occurs in mandible 60% of time and usually 5th to 6th decade.	Lining of the cyst may be squamous, cuboidal, or columnar.	Surgical excision and microscopic evaluation	Complete removal is needed and a definite confirmation.
Dentigerous cyst (Follicular cyst)	Odontogenic; develops from the dental follicle following crown formation. There is fluid between the crown and reduced enamel epithelium.	Always associated with the crown of an impacted or unerupted tooth, supernumerary tooth, or odontoma.	Male predilection, with most occurring in the mandible. It is the most common odontogenic developmental cyst in young adults, and the second most commonly occurring odontogenic cyst overall.	Lining consists of nonkeratinized epithelial lining composed of stratified squamous epithelium. The lesion is unilocular and well circumscribed.	Complete removal by enucleation or curettage with follow-up.	May displace teeth when it becomes large. Early diagnosis is crucial. Slight risk of recurrence of other tumors such as ameloblastoma or mucoepidermoid carcinoma.
Eruption cyst Palatal cyst of the newborn	Occur at the alveolar ridge with blood or fluid between the crown of an erupting tooth. Usually trauma induced.	Always associated with an erupting tooth. When found in the junction of the hard and soft palate, they are termed Bohn nodules. These are small cysts. Epstein pearls occur along the median palatal raphe. They are from trapped epithelium in the line of fusion.	No gender predilection	Fluid and blood. Identification through histology is not performed.	Sometimes the cyst is lanced to speed the eruption process in the case of a developing tooth.	No follow-up needed unless eruption does not proceed as planned. Parents are often concerned with the appearance of the eruption cyst.
Odontogenic keratocysts (OKC) (keratocystic odontogenic tumor)	The source is the dental lamina and probably the stimulation of the rests of Malassez and Serres.	Aggressive odontogenic cyst. Occur most often in the ramus and mandible. Can destroy tissue and bone. Teeth may be displaced.	Equal sex distribution. Third most common odontogenic cyst. May be unilocular (round or ovoid) or multilocular radiolucency with a scalloped contour. Third most commonly occurring odontogenic cyst.	The cyst produces daughter cells (islands of epithelium) and out-pouchings. The cyst has a thin epithelial lining with fewer than six cell layers.	The cysts are locally destructive. They tend to recur. Teeth may be displaced in some cases. May have radiographic appearances similar to other types of cysts. Histological differentiation is crucial. Nevoid basal cell carcinoma syndrome should be considered.	There is a high rate of recurrence, so patient should be monitored for this. Recurrence usually takes place within the first 5 years after removal.
Nevoid basal cell carcinoma syndrome	Autosomal dominant disorder	Bifid rib, odontogenic keratocysts, skeletal abnormalities, palm and sole pits, and basal cell carcinoma	Occurs in wide age range, 1/57,000–1/256,000. Usually seen in whites.	Patients are predisposed to various neoplasms. Each variant is treated individually. Major and minor classifications are used depending upon the extent.	When seen in a dental office, a keratocyst or other neoplasm should be evaluated with the syndrome in mind. Early identification is crucial. Facial skin areas should be evaluated as well: hairline, neck (back of neck), etc.	Sunscreen and Vitamin A, D, may be helpful in the control of skin lesions.
Calcifying odontogenic cyst (Gorlin cyst)	Derived from the reduced-enamel epithelium	May resemble the gingival cyst or the peripheral giant cell fibroma.	Appear as unilocular to multilocular lesions. Have clearly defined margins. Mixture of calcifications and radiolucent areas.	Ghost cells that are made of keratin with the nucleus absent. May also resemble the ameloblastoma microscopically. Root divergence is often observed.	Complete removal is necessary. The neoplastic variety needs to be treated aggressively.	Recurrence is sometimes seen. Careful evaluation at maintenance appointment is needed.
Glandular odontogenic Cyst (GOC)	Derived from odontogenic origins. It is locally aggressive.	Rare; only 0.2% of all odontogenic cysts. No gender preference. Mean age is 51. Most occur in the mandible.	Well-defined unilocular or multilocular radiolucency involving the periapical area of multiple teeth. Some may appear scalloped. Swelling and expansion are noted. Pain, discomfort, infection, and paresthesia have been noted.	Microcysts, epithelial spears, clear cells, variable thickness of the lining and multiple compartments are of value. Eosinophilic cuboidal cells are present as well.	There is a high recurrence rate (50%) within 5.8 years after treatment.	Enucleation, curettage, cystectomy and excision.

continues

Chapter 20 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Nasopalatine canal cyst (incisive canal cyst, nasopalatine duct cyst)	Developmental. Derived from the epithelial remnants of embryonic structure.	Occurs in 1% of population. It is the most commonly occurring cyst that is not of odontogenic origin. May have a blue or red hue when in the soft tissue.	Size determines clinical facial swelling. Well circumscribed radiolucent lesion that may have a sclerotic border.	Lining is stratified squamous epithelium. Cyst is not radiographically diagnostic.	Complete surgical removal. Prognosis is good and the recurrence is low with complete removal.	Patient may complain of a salty taste, tenderness, swelling and drainage. When in the soft tissues of the incisive papillae, called cyst of the incisive canal.
Median palatine cyst	A fissural cyst; develops from entrapped epithelium in fusion line.	Located in the same vicinity as the nasopalatine cyst but more in the center of the palate.	Discovered on radiograph unless patient has begun to experience symptoms. Most frequently in young adults.	Lined by stratified squamous epithelium and surrounded by dense connective tissue.	Removal of the cyst through surgery	Patient may complain of pain and expansion.
Static bone cyst (Stafne bone defect, static defect)	Defect in the mandible that surrounds salivary gland tissue. It is not lined with epithelium and not a true cyst.	The bone cyst is probably present at birth and is a defect.	Discovered on radiograph usually. Seen in adults. Most are unilateral with clear distinct margins.	If the cyst appears above the mandibular canal, a biopsy needs to be taken. Otherwise, close follow-up is needed.	The area is usually asymptomatic. No treatment is needed.	Patient is made aware of the lesion and is evaluated at future maintenance appointments.
Adenomatoid odontogenic tumor (AOT)	Considered a neoplasm and a benign epithelial tumor	The entity is encapsulated with a dense fibrous capsule. As tumor enlarges, a hard bony eggshell-like appearance is noted over the protrusion.	Usually affects age ranges from 5–30 years old. Average age is 20 years. There is a female predilection of 2:1. Anterior maxillary (canines) are favored. Many are associated with impacted teeth.	Root displacement is common when the AOT expands. The tumor appears radiolucent with foci within the tumor. The glandular or duct-line histology features form a rosette pattern. These are composed of columnar epithelial cells.	Facial asymmetry is one of the first signs of this tumor. Complete removal is needed and recurrence is not noted. The lesion is encapsulated and does damage through expansion.	Maintenance and follow-up is needed. Periodic radiographs should be taken.
Odontogenic myxoma	Originates from the periodontal ligament (PDL) or dental pulp	Nonencapsulated, persistent neoplasm capable of rapid growth.	Affects age ranges of 10–30 years old. No gender predilection and seen in both arches.	Root displacement and resorption is common. The tumor may be confused with other entities and other myxoid jaw neoplasms.	The tumor is difficult to remove because it is non-encapsulated and may have spillage of the gelatinous material making recurrence possible. Care should be taken to reevaluate the area at maintenance appointments.	Maintenance and follow-up is needed. Periodic radiographs should be taken.
Ameloblastic fibroma (fibro-odontoma)	Rare mixed odontogenic tumor. Believed to originate from ectomesenchyme and odontogenic epithelium.	Associated with unerupted teeth	Affects those under age 20 most frequently. Some reported in third and fourth decades. No gender preference.	Unilocular or multilocular, and well defined. Composed of long strands and islands of odontogenic epithelium. Tall columnar cells. Calcified material containing dentin and enamel may be seen on occasion.	Conservative excision is the treatment of choice. Recur at rate of 20%. The patient experiences no pain with swelling. Lesion may cause jaw expansion.	Maintenance and follow-up is needed. Periodic radiographs should be taken.
Langerhans cell disease (previously called histocytosis X)	Proliferation of Langerhans cells	Involves three distinct variants of the disorder: eosinophilic granuloma, Hand-Shuller-Christian, and Letterer-Siwe disease.	Usually involves young adults under the age of 10 years old.	Punched out lesions are noted on radiograph in skull with all bones affected. Bones of mouth affected and result in "floating teeth." Birbeck granules are evident in histology specimen.	Early diagnosis is crucial since the more widespread the disease states, the more difficult to treat. Prognosis is better when found in an older patient. Lymphadenopathy is observed. Chemotherapy and surgery are options. Bone marrow transplants may be needed as well.	Maintenance and follow-up is needed.

CHAPTER 21

Abnormalities of the Teeth

KEY TERMS

Autosomal
Coloboma
Coronal
Dominant
Ectoderm
Follicular
Gastroesophageal reflux
Heterozygous
Hiatal hernia
Homozygous
Kindred
Parafunctional
Pathognomonic
Penetrance/penetrant
Percussion
Prophylactic
Radicular
Recessive
Stellate reticulum
Tensile strength
Venereal disease (sexually transmitted disease [STD])
X-linked

LEARNING OUTCOMES

1. Define and use the key terms listed in this chapter.
2. List the three main categories of traumatic influences that produce an alteration in the appearance of the teeth and note how they can be differentiated from one another.
3. Discuss the characteristic clinical features associated with a pulp polyp.
4. Describe the differences seen in the radiographs that help to distinguish internal resorption from external resorption.
5. Describe the clinical presentation of inflammatory induced enamel hypoplasia and how it differs from the developmental abnormalities that affect enamel formation.
6. Note the location of the most commonly missing tooth and discuss the genetically linked syndrome that is associated with multiple missing teeth.
7. Discuss hyperdontia and note the genetically linked syndrome associated with a markedly increased number of teeth (above the normal number of 32).
8. Note the tooth (other than the third molar) that is most commonly affected by microdontia.
9. Discuss the primary clinical concern when performing an occlusal adjustment on teeth affected with talon cusp or dens evaginatus.
10. List the pertinent radiographic features that allow distinction of gemination from fusion.
11. Define enamel pearl and note the common dental condition for which it may be mistaken.
12. Discuss the disease process involved with excessive hypercementosis on multiple teeth.
13. Describe the radiographic features associated with amelogenesis imperfecta and dentinogenesis imperfecta.
14. List four conditions that alter the structure of teeth and may lead to the development of periapical radiolucent lesions without an obvious cause being seen in the tooth crown.
15. Note the scientific names for the alteration in tooth structure described as “rootless teeth” and “ghost teeth.”
16. State the level of fluoride concentration in the drinking water at which dental fluorosis typically occurs.
17. Discuss how tetracycline may be associated with discoloration of the teeth when administered during the period of tooth formation.

CHAPTER OUTLINE

Postdevelopmental Abnormalities of the Teeth
- Traumatic Conditions
  - Attrition
    - Abfraction
  - Abrasion
  - Erosion
- Inflammatory Conditions
  - Pulpitis
    - Reversible Pulpitis
    - Irreversible Pulpitis
    - Hyperplastic Pulpitis
  - Pulp Stones
    - Internal Resorption
    - External Resorption
  - Enamel Hypoplasia

Developmental Abnormalities of the Teeth
- Alterations in the Number of Teeth
  - Decreased Number of Teeth/Anodontia
  - Decreased Number of Teeth Associated with Syndromes
    - Hereditary Hypohidrotic Ectodermal Dysplasia
    - Incontinentia Pigmenti (Bloch-Sulzberger Disease)
  - Increased Number of Teeth/Hyperdontia
  - Increased Number of Teeth Associated with Syndromes
    - Cleidocranial Dysplasia (Dysostosis)
    - Gardner Syndrome
    - Other Syndromes Exhibiting Hyperdontia
- Alterations in the Size of Teeth
  - Decreased Size of Teeth/Microdontia
  - Increased Size of Teeth/Macrodontia
- Alterations in the Shape (Morphology) of Teeth
  - Abnormalities Affecting The Crowns of Teeth
    - Shovel-Shaped Incisors
    - Accessory Cusps
    - Gemination
    - Fusion
    - Congenital Syphilis
    - Lobodontia
    - Globodontia
  - Abnormalities Affecting the Roots of the Teeth
    - Accessory Roots (Supernumerary Roots)
    - Dilaceration
    - Enamel Pearl
    - Taurodontism
    - Concrescence
    - Hypercementosis
- Alterations in the Structure of Teeth
  - Enamel Hypoplasia
  - Amelogenesis Imperfecta
  - Dens Invaginatus (Dens in Dente)
  - Dentinogenesis Imperfecta (Hereditary Opalescent Dentin)
  - Dentinal Dysplasia ("Rootless Teeth")
  - Regional Odontodysplasia ("Ghost Teeth")
  - Vitamin D–Resistant Rickets (Hypophosphatemia)
  - Hypophosphatasia
- Alterations in the Color of Teeth
  - Fluorosis
  - Tetracycline Staining
  - Hemolytic Anemia and Erythroblastosis Fetalis
  - Porphyria (Congenital Erythropoietic Porphyria)

RELATED CLINICAL PROTOCOLS

#3 Maintenance Appointment Guidelines for the Patient with a Mucosal Disorder
#4 Treating Patients with Xerostomia
#9 Preventing Further Oral Tissue Damage in Patients with Eating Disorders
#10 Patient Education: UVA/UVB Skin Protection
#14 Postoperative Instructions for Oral Surgery Patients
#15 Office Protocol for Identifying Suspected Family Violence
#23 Oral Health Care Management for the Pregnant Patient
#25 How to Utilize Nutrition Counseling in Practice
#27 Motivational Interviewing for Behavior Change

Pathologic changes affecting the teeth may be caused by (1) genetic influences, (2) environmental factors, (3) disease processes, (4) metabolic disturbances, or (5) nongenetically linked defects in the normal development and growth of the teeth. In most cases, the pathologic process will produce clearly visible evidence in the teeth that heralds the presence of an abnormality. In some cases, however, the teeth may appear entirely normal on casual observation, and additional clinical correlation or microscopic evaluation of the teeth may be necessary to identify the nature of the process.

Pathologic changes affecting the teeth can be grouped into two broad categories: (1) changes occurring during the initial growth and development of the tooth (developmental abnormalities) and (2) changes occurring after tooth development when the tooth has completely erupted into the oral cavity (postdevelopmental abnormalities). The abnormalities that occur during the initial growth and developmental process are by far the more numerous. The abnormalities that occur following tooth eruption are relatively few and are typically limited to the traumatic and inflammatory categories.

Postdevelopmental Abnormalities of the Teeth

Traumatic Conditions

Attrition

Attrition is defined as the wearing away of tooth structure caused by tooth-to-tooth contact. Some attrition occurs in all individuals over the course of time as part of the normal functional aging process. It is produced by the ordinary

forces of occlusion and the abrasive stresses of mastication. The areas most affected by attrition are the occlusal surfaces of the posterior teeth and the incisal edges of the anterior teeth. Attrition also occurs at the interproximal contact points of the teeth and, over time, can result in small reductions in arch length. Therefore, attrition should only be regarded as pathologic when the loss of tooth structure is severe and out of proportion to expectations considering the age of the patient.

Certainly, the nature of the individual diet must also be considered, as it will affect the amount of attrition seen in a particular patient. Diets high in coarse, unrefined foods can be expected to produce greater attrition. Excessive grinding of the teeth (bruxism) and other **parafunctional** dental habits have also been implicated in severe attrition. Environmental factors may also play a role in the rate and extent of attrition. For example, people exposed to abrasive aerosols, such as those living in sandy desert climates, may show increased attrition relative to other populations. Attrition may be accelerated when developmental abnormalities affecting the surface hardness of the teeth are present. Abrasion and erosion (see below) are often seen in conjunction with attrition and can increase the severity of the loss of tooth structure.

Attrition can typically be recognized by a flattening of the normal rounded contour of the tooth in the affected area (Fig. 21.1). The surface of the flattened area usually appears burnished or polished relative to the adjacent unworn tooth surface. The area of faceting will show direct contact with an occluding tooth in the opposite dental arch. Even when excessive, attrition rarely causes symptoms for the patient, although occasionally a patient may complain of thermal sensitivity. The process proceeds at a slow enough rate to allow deposition of secondary dentin, insulating the dental pulp from noxious stimuli.

Abfraction. Abfraction is considered a subcategory of attrition by some authors, but the concept is not universally accepted as a cause of loss of tooth structure. Abfraction is defined as the loss of tooth structure in the cervical neck area of the teeth, which is produced by the transmission of forces generated during occlusion and mastication (chewing). Dentin is known to have a greater **tensile strength** than enamel. Because of this greater tensile strength, when stresses are applied to the tooth during occlusion and mastication, the dentin is better able than enamel to deform and rebound to its normal shape. This produces stress along the dentinoenamel junction. At the cervical area of the tooth, the enamel thins considerably as it curves inward to abut the root surface. Thus, this combination of curvature, thinning of the enamel, and flexing of the dentinoenamel junction with the application of occlusal forces is theorized to produce cracking within the crystalline rod–like enamel structure. With repeated stresses, the enamel may eventually separate from the dentin completely and be lost. Abfraction typically appears as wedge-shaped areas of enamel loss. It is hypothesized to occur more often when the forces of occlusion are applied eccentrically, such as occurs in lateral jaw movements or in the grinding pattern associated with bruxism.

FIGURE 21.1. Attrition. Note the short height of the clinical crowns of the anterior teeth in both the maxilla and mandible. There is also flattening of the canine and premolar cusp tips.

Abrasion

Abrasion is defined as the pathologic wearing away of tooth structure due to external factors that are mechanical and usually frictional. It typically occurs in the setting of a regularly repeated action performed over a long period of time. Inappropriate toothbrushing is probably the most common cause of abrasion. Increased attention to patient oral hygiene habits by dental professionals, accompanied by advocacy of the use of soft bristle toothbrushes and the development of less abrasive toothpastes has decreased the incidence of this type of abrasion; however, it still is seen with some frequency. Since cementum is softer and less resistant to abrasion than enamel, the exposed root surfaces in patients with gingival recession or periodontal disease are the most prone to develop this type of abrasion. It usually presents as a linear, V-shaped, or U-shaped depression in the tooth structure just above the free gingival margin. The defect tends to be oriented parallel to the occlusal surface of the involved tooth.

Abrasion may be produced by other individual habits, which may be related to the patient's occupation. In this situation, the abrasion is associated with the use of the teeth as a "tool" or to assist the individual in repetitive tasks related to his or her job (Fig. 21.2). Thus, hairdressers (opening bobby pins), carpenters (holding nails), tailors and seamstresses (holding pins and needles, biting thread), and electricians (stripping electrical wire) among others have been reported to show an increased incidence of abrasion. When abrasion is occupation associated, it is often seen to primarily affect the anterior teeth and it may be limited to a single tooth in each arch. Nonoccupational habits often reported to be associated with abrasion include pipe smoking, tobacco chewing, and misusing other dental hygiene aids, such as dental floss and toothpicks.

FIGURE 21.2. Abrasion. Distinctive notching of the maxillary and mandibular central incisors. The patient was an electrician and used his teeth to strip protective plastic covering from electrical wire.

As with attrition, developmental defects that alter the composition or hardness of tooth structure may predispose a patient to develop abrasion. In addition, the rate of loss of tooth structure may be more rapid. Even when abrasion occurs over a relatively short period of time, patients are seldom symptomatic.

Erosion

Erosion is defined as the loss of tooth structure produced by the contact of chemical agents with the tooth. Dental caries, although produced by the acidic by-products of the activity of oral bacteria, is a separate category of disease and is not considered a form of erosion. Highly acidic foods and liquids are most often implicated in the production of erosion, but other chemicals have occasionally been shown to produce it. Chelating agents, such as EDTA, have specifically been implicated. Susceptibility to erosion, at least in part, is influenced by the quantity and quality of salivary flow. Normal saliva contains bicarbonate, which has a natural buffering effect, reducing the acidity of materials that pass through the oral cavity. Also, since prolonged and repeated contact of the acidic materials with tooth structure is customarily required for erosion to occur, adequate salivary flow should hinder erosion by diluting and washing the acidic materials away from contact with the tooth. In fact, saliva is known to facilitate remineralization of enamel surfaces that show early erosion or carious involvement. Thus, patients with decreased salivary flow would be expected to show an increased incidence of erosion and loss of tooth structure.

Despite the generally protective effects of saliva, patients with normal salivary flow may still show evidence of erosion. This may be due to idiosyncrasies in the individual diet, personal habits, or medical conditions. In all instances though, the quantity of acidic material is so great that it overwhelms the ability of the saliva to compensate. Ingestion of large quantities of sugar-containing carbonated beverages has been implicated as a significant etiologic factor. Citrus fruit and juices are other potential sources of highly acidic material. In one instance, severe erosion of the maxillary and mandibular teeth was noted in a patient who would habitually suck on a lemon wedge held against the anterior teeth by the lips. Another unusual case highlights erosion seen in competitive swimmers who practiced daily for long periods in a swimming pool with inadequately controlled pH. Medical conditions that predispose a patient to repeated episodes of vomiting are additional etiologic factors in the production of erosion. The best known and most often reported of these is anorexia nervosa/bulimia, but pregnancy and alcoholism are also established as potential factors. **Gastroesophageal reflux** and **hiatal hernia** likely account for a small number of cases as well. When erosion is produced by contact with gastric secretions, it is termed "perimolysis." As with attrition and abrasion, concurrent developmental defects affecting the hardness of tooth structure may accelerate the process of erosion.

Clinically, erosion may resemble attrition and abrasion to some extent, producing a smooth and polished-appearing depression in the tooth surface. Multiple teeth are normally affected. Unlike attrition, it does not tend to be seen in areas where there is occlusal contact of the teeth, although severe cases of erosion may involve occlusal surfaces. Erosion may be distinguished from abrasion, since it typically produces a broader and more rounded area of depression than the linear, V-shaped areas that typify abrasion (Fig. 21.3). However, since erosion may predispose to abrasion by softening the tooth surface, the two processes are often seen in concert. While erosion may be seen on

FIGURE 21.3. Erosion. Note the diffuse flattening of the exposed root surfaces on the facial surface of the premolar and molar teeth. The patient placed smokeless tobacco in this area regularly over a prolonged period. Some abrasion from the rough texture of the smokeless tobacco is also present.

any tooth surface, it typically is found in the gingival third area of the teeth where the normal periodontal architecture may provide a somewhat protected environment for prolonged contact of the chemical agent with the tooth surface. The root surface and cementoenamel junction areas of the teeth are most susceptible to the effects of erosion. In general, erosion associated with acidic dietary foods and liquids tends to affect the labial and buccal surfaces of the teeth more prominently, while erosion associated with repeated vomiting is seen to produce more damaging effects on the lingual and palatal surfaces. Thus, the areas of involvement with erosion may produce significant clues about the cause of erosion. Another prominent diagnostic sign associated with erosion is protrusion of amalgam restorations above the level of the surrounding tooth structure. In this scenario, the metallic amalgam restoration is immune to the effects of the chemical agent, while the surrounding tooth structure is eroded, producing the characteristic "elevation" of the filling material. In severe cases of erosion, thermal sensitivity may be reported, but many patients are entirely asymptomatic.

Inflammatory Conditions

Pulpitis

By definition, pulpitis is inflammation involving the dental pulp. Pulpitis is exceedingly common, and nearly every individual will suffer symptoms of pulpitis at some time during his or her life. The inflammation within the dental pulp may be produced by a variety of stimuli. Dental caries is the most common. External trauma, trauma from occlusion and mastication, invasive and noninvasive dental procedures, and extreme temperature changes may produce pulpitis as well. Attrition, abrasion, and erosion are occasionally implicated. The involved tooth may show an obvious source for the pulpal inflammation (e.g., carious lesion, fracture) or it may appear entirely normal clinically. Unless pulpal necrosis has occurred with spread of the inflammatory process through the root apex and into the **radicular** bone, radiographs will appear normal. Occasionally, teeth affected by pulpitis will show a slight widening of the periodontal ligament space at the apical region of the tooth. Therefore, in many instances, pulpitis can only be recognized by the symptoms reported by the patient (i.e., a toothache).

Pulpitis can be divided into three subcategories: reversible pulpitis, irreversible pulpitis, and hyperplastic pulpitis. These three subcategories have clinical features that usually allow rapid and dependable diagnosis.

Reversible Pulpitis. In reversible pulpitis, as the name indicates, it is expected that the inflammation of the pulp will resolve and the tooth will eventually return to a normal condition. Pain is the presenting symptom, and it typically is instigated by cold only. Heat may elicit the pain on occasion but usually not without cold sensitivity being present as well. In very rare instances, sweets or tart food may initiate the pain, but **percussion** of the tooth (striking a tooth with short, sharp blows to elicit pain) normally does not. The pain is not usually described as severe but is sharp. A particularly distinctive characteristic of reversible pulpitis is that the pain is very sudden in onset with application of the stimulus and almost as sudden in disappearance once the stimulus is discontinued. The total duration of the pain is classically described as only a few seconds following stimulus removal. An inciting stimulus for the pain is a required criterion, as the pain associated with reversible pulpitis is never spontaneous.

Irreversible Pulpitis. If the inflammation of the dental pulp persists, the condition may progress from reversible to irreversible pulpitis. The hallmark feature of irreversible pulpitis is the presence of pain that lingers or is continuous following removal of an inciting stimulus. Pain may still be initiated by cold but is also more reliably produced by heat, among other stimuli. In contrast to reversible pulpitis, the pain may be initiated only by heat without corresponding cold sensitivity. The pain is more often described as severe, in addition to being sharp, and it may worsen when the patient lies down. Percussion of the tooth may elicit the pain response. In irreversible pulpitis, an initiating stimulus for the pain is not always necessary, and spontaneous onset of pain, in particular, heralds the presence of irreversible inflammatory changes. Once the inflammation in the dental pulp has progressed to irreversible pulpitis, endodontic therapy becomes necessary.

Hyperplastic Pulpitis. Hyperplastic pulpitis, often referred to as chronic hyperplastic pulpitis, is a form of pulpitis with a characteristic clinical presentation. It has also been termed pulp polyp. It is always seen in association with a tooth that has a large carious lesion. The deciduous and permanent molar teeth are the most commonly involved, and patients tend to be children, adolescents, or young adults. The carious lesion almost always involves a major portion of the occlusal surface and has progressed to the point of destroying the roof of the underlying pulp chamber, exposing the pulp tissue to the oral environment. The pulpal tissue is irritated and inflamed. However, because the roof of the pulp chamber has been destroyed by the carious process, the pulp tissue is able to expand in response to the inflammation, unlike the other forms of pulpitis in which the irritated and inflamed pulp tissue is nearly completely enclosed by dentin. Thus, the pulp tissue is able to become hyperplastic, with a mass of granulation tissue welling up out of the pulp chamber. Clinically this presents as a bright red, dome-shaped mass of tissue occupying the carious defect in the occlusal surface. Pain is usually not present, although occasionally patients complain of some sensitivity when they try to chew on the affected side. However, touching the surface of the dome-shaped red lesion with the tip of an explorer may elicit a sharp, stabbing pain and bleeding. Treatment requires endodontic therapy or extraction.

Pulp Stones

Pulp stones are abnormalities of the teeth that, for the most part, are clinically insignificant. However, they are occasionally noticed in dental radiographs, usually as

APPLICATION 21.1

Monitoring the brushing habits of young children is an important aspect of how well the young child escapes the ravages of dental caries, fluorosis, and tissue damage. Obtaining the optimal oral health for their child is the goal of all parents. Studies have indicated that there may be wide disparity in what parents report as the overall time spent brushing, the amount of dentifrices used, the exposure to fluoride, rinsing during brushing, and rinsing as a final procedure. Researchers report that the window of maximum susceptibility to the occurrence of fluorosis is the first 3 years of life. Sources of fluoride intake include drinking water, using fluoride toothpaste, dietary fluoride supplements, and infant formulas. Additionally, another consideration is the type of toothbrush that may be used such as a manual brush or an electric toothbrush. It has been documented that some children (even under the age of 5 years old) use the small, nonelectric, devices that may be carried from room to room. Children have been reported to sit in front of a television set and to leave the rotating brush in one area of the mouth without moving it around and consistently maintaining this habit for long periods of time. This causes damage to the soft tissue and may abrade the tooth enamel over time. Parents should be asked about brushing habits of their children, but researchers caution the information from parents/caregivers may often be quite removed from what actually occurs. Relevant questions and suggestions that need to be addressed are as follows:

1. Is the water fluoridated?
2. Is the parent present while the child is brushing?
3. Is a timer used to assist in brushing? This gives the child an indication of how long to spend using a brush with supervision.
4. Is the child using a manual or electric toothbrush? Young children should not use an electric brush without supervision. Manual brushes work well for young children.
5. Is the child using the appropriate amount of paste? The dental professional may give guidelines on the amount of paste in addition to the type of toothpaste that is recommended.
6. Does the child rinse thoroughly after brushing since the toothpaste should not be swallowed? Some children like the taste (especially the highly flavored ones, e.g., bubble gum and fruit flavorings) and have been known to eat toothpaste when not supervised.
7. Instructions in the proper technique of brushing should be given to both the parent and to the child. This is an element that should be reinforced at each visit; providing printed information that the parent can refer to is optimal.
8. Pregnant women may ask about fluoride and the use of infant formulas that may contain fluoride. Familiarity with these products should be part of your office protocol. Local pediatricians and pediatric dentists can be a good resource for current information and current theory.

Giving general information about brushing for young children should be a standard office protocol with a consensus of others employed in your office resulting as standard of care information.

Develop patient education information for each of the topics mentioned above. The information allows your office to answer many of the questions that will arise related to products, brushing, and fluoride use. This approach also stimulates discussion and provides needed updates.

Buzalaf MA, Levy SM. Fluoride intake of children: considerations for dental caries and dental fluorosis. Monogr Oral Sci 2011;22:1:1–19.

Martins CC, Oliveira MJ, Pordeus IA, et al. Comparison between observed children's tooth brushing habits and those reported by mothers. BMC Oral Health 2011;11:22.

an incidental finding. On the radiograph, they present as round-to-oval areas of opacity within the radiolucent area that defines the pulp chamber or root canal space (Fig. 21.4). Unless there is another reason for inflammation involving the dental pulp, the teeth that show pulp stones are predictably asymptomatic. The etiology of pulp stones is not known with certainty. Studies done in the first half of the 20th century suggest that the formation of pulp stones may be a physiologic process representing the normal aging process of the dental pulp. These studies showed that the incidence of pulp stones increased with advancing age of the patient, with more than 90% of teeth examined in the 50- to 70-year-old age group showing some evidence of pulp stone formation. The actual mechanism of pulp stone formation is also uncertain but is theorized to involve calcification around a nidus of altered cells within the pulp tissue. The most likely cause of the cellular alteration appears to be inflammation of the pulp tissue. Since pulp stones are clinically innocuous and are most often discovered as an incidental finding, no treatment is necessary. The only significant untoward effect of pulp stones occurs when a

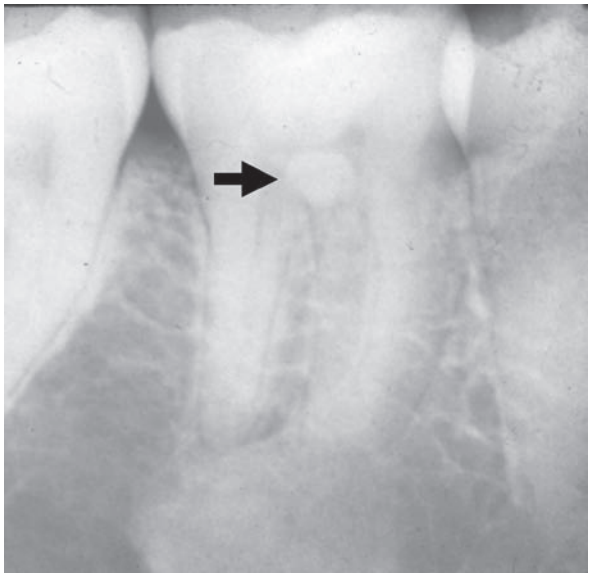
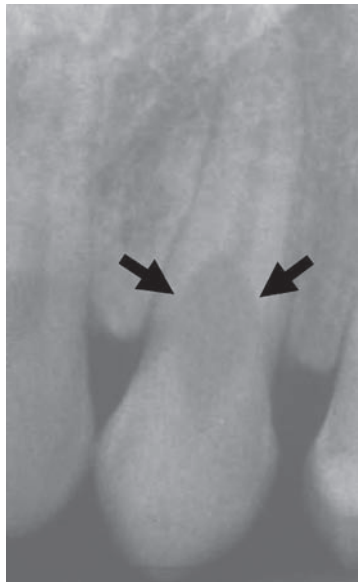


FIGURE 21.4. Pulp stone. A rounded area of radiopacity is seen within the pulp chamber of the molar tooth. Note the large restoration encroaching on the dental pulp as a likely source of pulpal inflammation.

particularly large pulp stone interferes with conventional endodontic procedures.

Internal Resorption. Internal resorption is defined as the destruction of tooth structure that is initiated from within the pulp chamber or root canal. This is a rare occurrence compared to the far more frequently observed process of external resorption (discussed below). Usually, a single tooth is affected. While the exact cause of internal resorption is not known in all cases, a significant number of cases are believed to result from injury to the pulp tissues. This injury causes an influx of inflammatory cells, some of which transform into osteoclast-like cells that then destroy the dental hard tissue from within (Fig. 21.5A). Dental caries and traumatic episodes have been most often implicated in initiating the inflammation. The resorptive process may stabilize and remain at a fixed size or it may be progressive, eventually perforating the external tooth surface unless treatment intervenes.



A

B

FIGURE 21.5. Internal resorption. **A**. Note the bulbous radiolucent enlargement of the pulp. **B**. *Pink* discoloration of the crown is due to enlargement of the pulp chamber associated with internal resorption.

Teeth affected by internal resorption are usually asymptomatic. Most are discovered as an incidental finding in a radiograph taken for some other reason. The resorption presents as a bulbous radiolucent enlargement of the pulp that is commonly symmetric and clearly visualized against the surrounding opaque tooth structure. The margins of the lucent area are often sharply defined but may be hazy. The resorption is seen most often in the cervical neck area of the tooth at the level of the cementoenamel junction; however, it can occur anywhere within the pulp system. If it involves primarily the **coronal** pulp chamber, thinning of the dentin may occur to the extent that the highly vascularized pulp tissue can be visualized through the translucent enamel. The crown of the tooth exhibits a pink to light red discoloration (Fig. 21.5B). This presentation is sometimes referred to as the "pink tooth of Mummery" and is considered diagnostic for internal resorption. Teeth affected by internal resorption can be successfully treated with endodontic therapy in many cases. Once perforation of the external surface has occurred, treatment options are more limited, and extraction is regularly the treatment of choice. Heroic attempts at restoration of the area of perforation have been attempted with varying results.

External Resorption. External resorption is defined as the destruction of tooth structure that is initiated from outside the tooth. In contrast to internal resorption, it is commonly observed. In some studies, critical evaluation of large numbers of radiographs revealed some external resorption to be present in all patients. Thus, external resorption should not be considered a pathologic process unless a significant portion of tooth structure has been destroyed. The main impetus for external resorption is also thought to be trauma. However, a larger proportion of cases of external resorption have no identifiable causal factor. These cases are classified as idiopathic external resorption. Destruction of tooth structure in external resorption is believed to be initiated by cells that originate in the periodontal ligament. These cells differentiate into osteoclast-like cells to destroy the tooth structure. Numerous specific local factors in addition to trauma have been shown to be associated with external resorption, but they all can be divided, from an etiologic standpoint, into two categories: (1) conditions that generate inflammation on the external tooth surface and (2) conditions that produce pressure against the periodontal ligament. Conditions generating inflammation include periapical pathosis secondary to inflammatory pulpal disease, periodontal infections, periodontal treatment, endodontic treatment, surgical procedures (e.g., bone grafts, biopsy procedures, reimplantation of avulsed teeth), and some bleaching procedures. Specific infections have also been implicated, particularly herpes zoster. Conditions producing pressure against the periodontal ligament include pathologic processes (e.g., cysts, tumors, fibroosseous diseases, condensing osteitis), pressure from adjacent impacted or erupting teeth, orthodontic care, and perhaps even traumatic occlusion.

External resorption affects multiple teeth more commonly than does internal resorption, but involvement of only a single tooth also occurs. Any area of the tooth may be affected, although most cases involve the lower one-half of the tooth. Resorption of the crown is unusual unless the tooth is impacted or the resorption encroaches on the crown structure from an area of cervical involvement. When the cervical area of the tooth is involved, resorption can be exceptionally destructive and rapid, threatening to produce amputation of the crown. Radiographically, external resorption is generally characterized by an asymmetric radiolucency that has a ragged or "moth-eaten" border where it abuts against the tooth structure. Where the tooth structure is actively being destroyed, the lucent area may show variation in the degree of lucency, producing a mottled or mixed radiolucent–radiopaque appearance as shown in Figure 21.6A. Alternatively, some cases of external resorption manifest simply as loss of tooth root length. In this situation, a clearly defined radiolucent defect is not appreciated, and the tooth roots just seem abnormally short. The root tip area often seems blunted. This radiographic presentation of external resorption tends to be produced more commonly by processes that place pressure on the periodontal ligament. Treatment of external resorption depends entirely on the location of the resorptive defect, the amount of resorption, and the patient's symptoms. Obviously, any factors predisposing to resorption must be eliminated first. If the resorptive defect is in an accessible area, restorative procedures may halt the process. Large areas of resorption that significantly weaken the tooth or its surrounding support will usually necessitate extraction (Fig. 21.6B and C). External resorption that presents as shortening of the root without an associated radiolucent defect does not require any treatment as long as the tooth is not excessively mobile.

Enamel Hypoplasia

While most cases of enamel hypoplasia are linked directly to developmental abnormalities of the teeth, it is sometimes

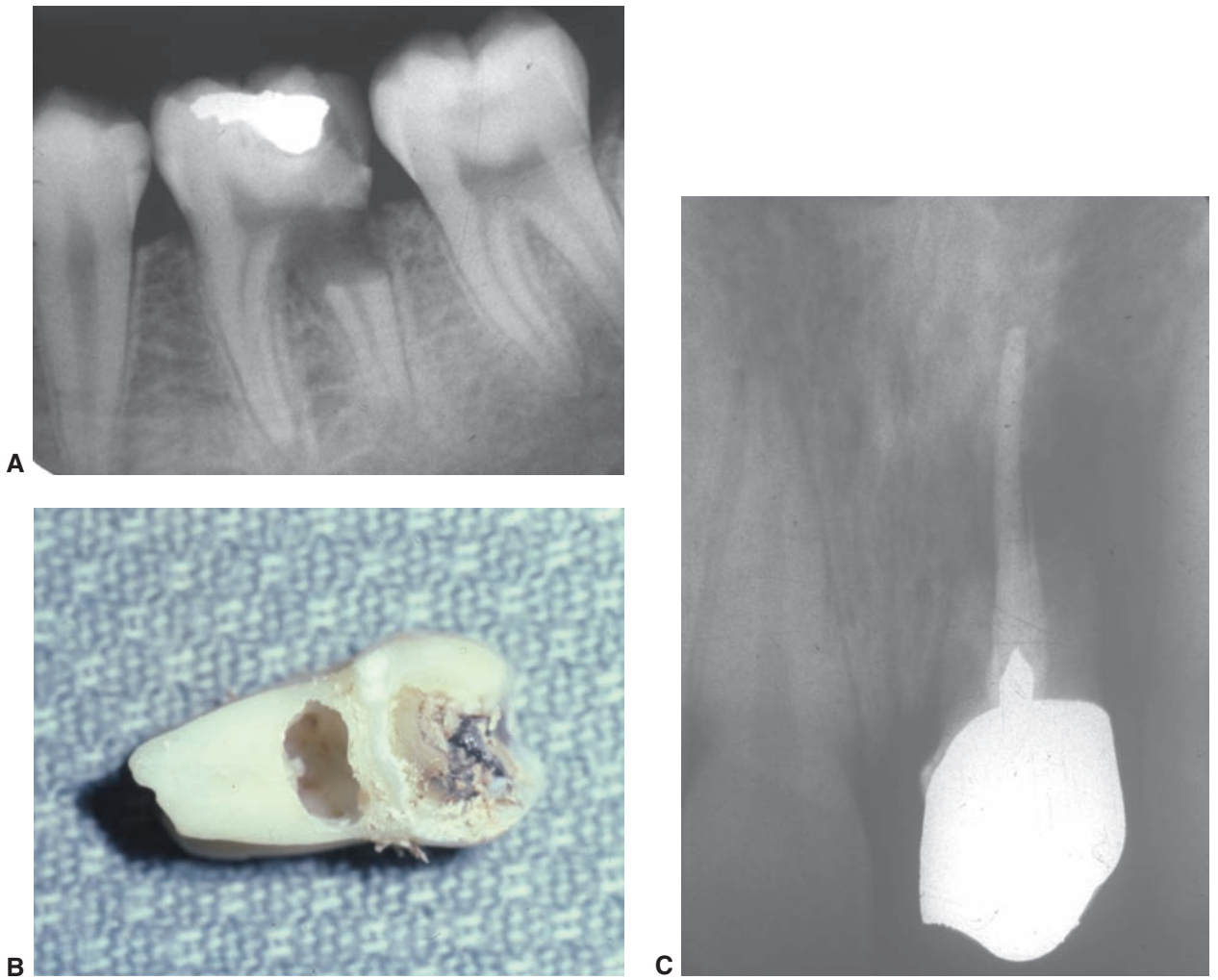


FIGURE 21.6. External resorption. **A.** The destruction has nearly amputated the distal root of the first molar tooth. **B.** Gross specimen of extracted tooth shows the extent of destruction of tooth structure. Soft tissue has been cleaned from the resorptive defect. **C.** Another case shows the extent of resorption possible. Nearly the entire hard tissue of the root has been resorbed, and the tooth was highly mobile, being retained in the alveolus only by the endodontic filling material. The patient gave a history of severe trauma to the tooth many years previously.

produced by inflammation. The inflammation involves the **follicular** tissues that surround the crown at the time of production and/or calcification of enamel matrix. This type of enamel hypoplasia is almost always seen involving premolar teeth, although it can affect any of the permanent teeth that have a deciduous tooth precursor. Permanent molar teeth are rarely affected. The deciduous tooth develops a periapical inflammatory lesion, which is most often a periapical abscess secondary to a carious lesion. Traumatic injury to the deciduous tooth, particularly of the type that tends to drive the tooth into the alveolar bone, has also been implicated as a causative factor. The crown of the permanent tooth, developing immediately beneath the roots of the deciduous tooth, becomes engulfed in the noxious environment produced by the periapical inflammation, injuring the enamel-forming cells of the tooth bud. The severity of involvement of the developing tooth crown can be quite variable and depends on the size, extent, and duration of the infection; the individual resistance of the patient; and the stage of growth of the involved developing tooth. This explains why the anterior teeth (incisors and canines) are so rarely involved. The anterior permanent teeth begin crown development shortly after birth, and enamel formation is complete by about age 5. Since the anterior deciduous teeth are less prone to develop carious lesions, the enamel on the underlying teeth is ordinarily fully formed before periapical inflammation can develop.

Inflammation-induced enamel hypoplasia most commonly affects only a single tooth, in contrast to developmental hypoplasia, in which multiple teeth are habitually involved. The involved tooth is often referred to as a Turner tooth. The degree of enamel hypoplasia can be minimal and difficult to recognize, presenting only as a discoloration of the enamel surface. This is typically seen when the initiating infection is mild or is successfully treated without delay. The hypoplasia can also be severe, producing considerable alteration of the normal crown form. In this situation, radiographic evidence of loss of enamel is evident. Most commonly, the hypoplasia presents as areas of pitting, grooving, or shallow cavitation, disrupting the normally smooth and shiny enamel surface. Large areas of loss of enamel may be seen. In some instances, small but multiple discrete areas of involvement on a single crown may be noted. If the enamel hypoplasia is severe or is unaesthetic, or the patient develops symptoms, restorative procedures remedy the situation in most cases.

Developmental Abnormalities of the Teeth

Alterations in the Number of Teeth

Decreased Number of Teeth/Anodontia

A decrease in the number of teeth is termed "anodontia." Anodontia may be complete or partial. Complete anodontia requires a failure of formation of all teeth, which is very rare. Partial anodontia is common and is defined as a failure of formation of one or more teeth as depicted in Figure 21.7. If six or more teeth are missing, the condition may be referred to as oligodontia. Hypodontia describes a situation in which one to five teeth do not develop.

Before classifying the absence of teeth as anodontia, the dental history of the patient must be considered, and a radiographic examination may be necessary. True anodontia

APPLICATION 21.2

Most patients are interested in obtaining the optimal aesthetic appearance for their teeth. The subject continues to be discussed in dental offices, and the dental professional must suggest the best possible procedure for the patient asking about bleaching approaches. Various types of products are on the market for both in-office whitening and for at-home whitening by the patient. Research continues to support the safety of these products when used as directed by the manufacturer. The various strengths of the products affect both the length of time they need to be used and the possible damage that may occur when the products are not used correctly. The accurate diagnosis of the cause of tooth discoloration is crucial. Some types of discoloration are more difficult to remove and others, such as tetracycline staining (which produces a gray color), may improve but never reach an acceptable level to either the patient or the dental professional. These discolorations may take much longer periods of bleaching over extended time periods but never reach an optimal outcome when compared to most patient results. Minocycline staining, often seen in patients who have been treated for acne, is somewhat easier to lighten, but patients should be made aware of the side effect of the long-term use of this antibiotic. When stains are caused by these products, in-office whitening procedures are needed with close monitoring. Europe requires that any bleaching product must be obtained through a prescription written by a dental professional. This allows close monitoring of the patient and also monitoring of the tissue. Stronger bleaching products may actually whiten and damage the soft tissues while being used. Most observable damage is reversed when products are discontinued. However, the literature suggests that in some individuals, there may be damage caused by free radicals or peroxides that may interact with DNA. Thus, carcinogenicity in some individuals may be of concern and certainly warrants monitoring. Short-term use of products may not fall into the same category, but with resistant stains, the length of time the tissue comes in contact with the products may be much longer. To date, there has been no scientific evidence for tissue changes related to bleaching and oral cancer.

Heyde M, Wilkins K, Li Y. Current trends in tooth whitening. Dimens Dent Hyg 2011;36–41.

Yiming L. Safety controversies in tooth bleaching. Dent Clin N Am 2011;55(2):255–263.

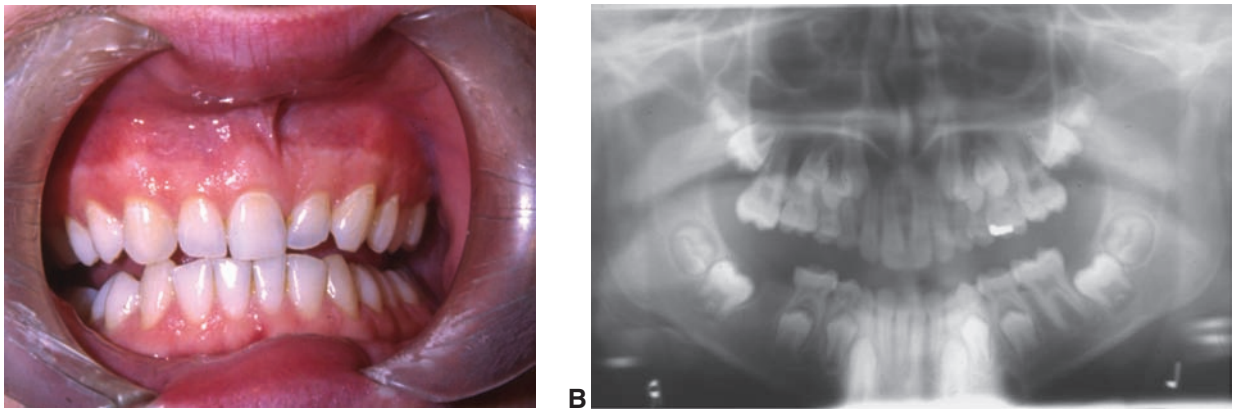


FIGURE 21.7. Partial anodontia. **A**. Only one maxillary central incisor tooth is present. The patient gives no history of tooth extraction in this area. (Photograph courtesy of Dr. Theodore Zislis.) **B**. The right mandibular first molar is missing. The other first molars are all present. There was no history of extraction or surgery in the right mandible.

is the failure of development of a tooth. The extraction of teeth may give the incorrect impression that teeth are developmentally missing. This condition is termed "false anodontia." An unerupted or impacted tooth may present as a clinically missing tooth with no dental history of prior extraction, also simulating true anodontia. Radiographs will prove that the tooth did develop appropriately. This is sometimes referred to as "pseudoanodontia."

Bilateral symmetry is commonly seen in anodontia, but on occasion, a single tooth on only one side of the jaws is absent. The teeth most commonly found to be developmentally missing are the maxillary and mandibular third molars. The maxillary lateral incisors are the second most commonly missing teeth. Mandibular second premolars are also often absent. The permanent first molar appears to be the least likely to be found developmentally missing. In the deciduous dentition, the maxillary lateral incisor is the tooth most commonly absent. In most cases when anodontia affects the deciduous dentition, the corresponding permanent successor also fails to form.

In most cases of anodontia, the lack of formation of the teeth is not associated with an identifiable systemic or genetic disease. However, some genetically inherited conditions are consistently connected with anodontia, and the failure of tooth formation may be the clinical characteristic that allows initial recognition of the associated syndrome.

Decreased Number of Teeth Associated with Syndromes

Hereditary Hypohidrotic Ectodermal Dysplasia. Ectodermal dysplasia is the most common of the genetic diseases that produce a decrease in the number of teeth. The oligodontia (discussed above) associated with ectodermal dysplasia is so striking that it is often the distinguishing feature that facilitates initial recognition of the genetic disease. A variety of genetic patterns of inheritance are known to exist. However, in most instances, it is an **X-linked** syndrome, meaning that the gene that produces the clinical manifestations is carried on the X (female) chromosome. In this form, it is also a **recessive** characteristic, since features of the disease are not seen in the patient if a normal gene is present on the matching X chromosome. However, males have only one X chromosome; thus, if they inherit a defective gene from their mother, they will show manifestations of the syndrome. Females are only seen to be affected when they inherit a defective gene from both parents, which occasionally occurs. Affected female patients are said to be **homozygous** for the disorder (both X chromosomes carry the defective gene), and the manifestations of the disease are particularly severe in this situation. Some **homozygous** females show almost complete anodontia. A female with one affected X chromosome and one normal X chromosome is a heterozygote. These patients typically do not show oligodontia, although sometimes they may be missing one or two teeth. Other manifestations of the disease are also typically absent in the **heterozygous** female. However, these women are carriers of the defective gene and can pass the disease on to their children. Most patients with hypohidrotic ectodermal dysplasia are, therefore, males.

As the name indicates, patients with hereditary hypohidrotic ectodermal dysplasia show defects of a variety of structures that are derived from the **ectoderm**. The skin is soft, smooth, and thin and seems dry. Teeth are ectodermally derived structures; therefore, in addition to exhibiting oligodontia, the teeth that do form in patients with ectodermal dysplasia are often misshapen. Cone-shaped anterior teeth are particularly common. Hair is another structure that is derived from the ectoderm, producing a distinguishing facial appearance. The scalp hair is very fine, blond, and sparse in distribution. Eyebrows and eyelashes are also sparse and may be nearly completely absent (Fig. 21.8). Interestingly though, most male patients develop a nearly normal facial hair distribution as they progress through puberty. For unexplained reasons, patients also typically have large, protruding, blubbery lips out of proportion to other facial features. Sweat glands are also affected by the genetic deficiency, and patients with ectodermal dysplasia may show heat intolerance due to their inability to lose

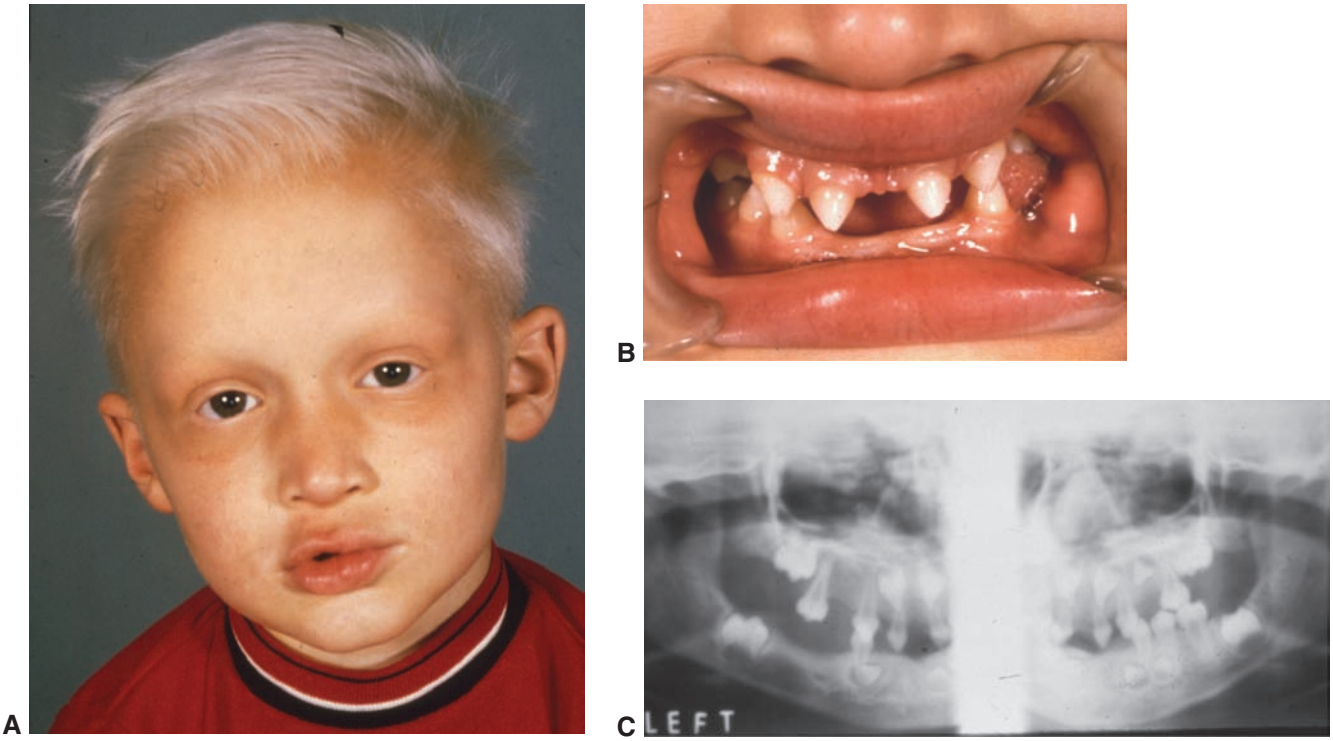


FIGURE 21.8. Ectodermal dysplasia. **A**. Young male patient shows characteristic facial appearance, with sparse fine blond hair, absence of eyebrows and eyelashes, and large lips. (Photograph courtesy of Dr. Robert Acterberg.) **B**. Intraoral clinical appearance of the same patient. Note multiple missing teeth. The anterior teeth have a cone-shaped crown morphology that is also commonly present in these patients. (Photograph courtesy of Dr. Robert Acterberg.) **C**. Panoramic radiograph of the same patient reveals an extensive number of congenitally missing teeth. (Photograph courtesy of Dr. Robert Acterberg.)

heat through the sweating mechanism. The failure of the salivary glands to form may be a component of the disease, and, when present, patients may complain of a dry mouth. This appears to be an uncommon manifestation; however, if it is present, the patient may be at increased risk of developing dental caries and periodontal disease.

Incontinentia Pigmenti (Bloch-Sulzberger Disease). Failure of formation of teeth is a characteristic associated with numerous other genetically linked diseases and syndromes. More than 30 syndromes are currently included on this list. In most of these diseases, the anodontia is a nominal component, with only a few teeth at most found missing, and the absence of the teeth does not usually contribute to the recognition of the disease process as it does in hereditary hypohidrotic ectodermal dysplasia. Incontinentia pigmenti seems to be the most likely of these diverse syndromes to produce a significant anodontia. Incontinentia pigmenti is also known as Bloch-Sulzberger disease. It is an **X-linked**, **dominant** genetic disease. As such, most patients are females. It is thought that the condition may be lethal in most males who inherit the defective gene, resulting in spontaneous abortion of the fetus or death during childbirth or in the early neonatal period. The disease manifests with skin abnormalities, neurologic disorders, and bone defects. The teeth are affected in 60 to 80% of patients. Partial anodontia is usual but not an overly prominent component. Peg-shaped anterior teeth are a common accompanying feature, and tooth eruption may exhibit a generalized delay.

Increased Number of Teeth/Hyperdontia

An increase in the number of teeth is termed "hyperdontia." It is a relatively common occurrence. The category of hyperdontia may be subdivided into supernumerary teeth and accessory teeth. Supernumerary teeth are additional teeth that at least approach the normal expected size of the adjacent teeth in the area. The crown form of a supernumerary tooth is usually identifiable as a specific class (i.e., incisor, canine, premolar, or molar). Supernumerary teeth tend to occur in specific sites within the jaws. While they can be multiple in a single site, they usually present as a single extra tooth per quadrant but show a significant propensity to bilateral symmetry with another supernumerary tooth being found in the same general location on the opposite side of the jaw. Accessory teeth, on the other hand, are diminutive, appearing as miniature replicas of a tooth. They often show a conical crown form rather than mimicking the occlusal form of the adjacent teeth, as is found with supernumerary teeth (Fig. 21.9).

Accessory teeth tend to occur with greatest frequency on the buccal or palatal aspect of the maxillary molar teeth. There may be multiple accessory teeth in one area, and while occasionally bilaterally symmetrical, they are more often limited to a single quadrant. Fusion of the accessory

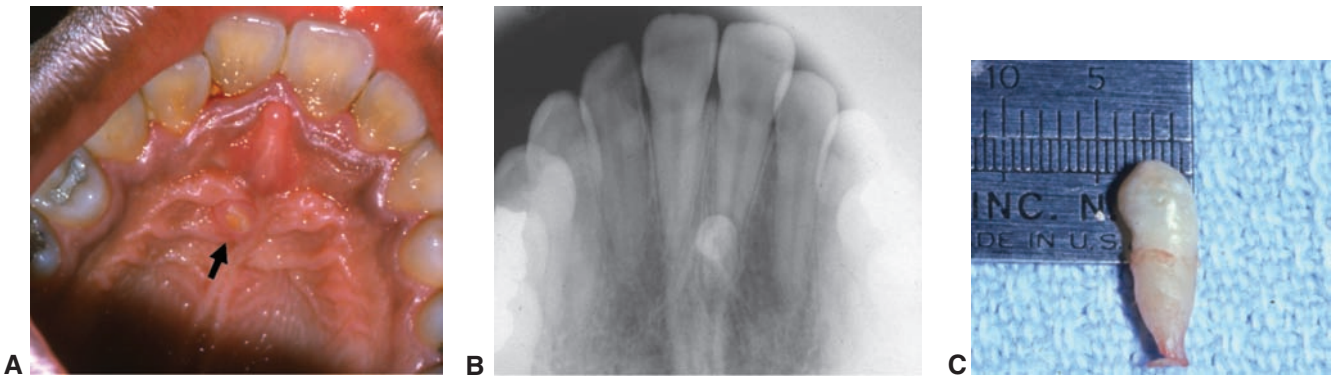


FIGURE 21.9. Accessory tooth. **A**. Clinical appearance of diminutive tooth in the rugae area of the hard palate. **B**. Occlusal radiograph of the accessory tooth seen in **A**. **C**. Extracted tooth as seen in **A** is only 4 mm in width.

tooth to the adjacent normal tooth occurs occasionally. Accessory teeth in the maxillary molar region are often referred to as "paramolars."

Statistically, the most common supernumerary tooth is the mesiodens. There is some evidence of **autosomal dominant** genetic inheritance associated with the presence of a mesiodens. It is found in the anterior maxilla, in many cases in the midline between the central incisor teeth. It presents as a single tooth most frequently, but occasionally, it occurs in pairs. It often presents with a peg-shaped or conical crown form rather than the typical appearance of a central incisor. Many mesiodens are impacted, and up to 50% of impacted ones appear upside down on periapical radiographs. In some instances, the mesiodens may erupt into the oral cavity, often on the palatal aspect. Early eruption of a mesiodens may block normal eruption of the permanent central incisor or cause significant crowding and malocclusion in the anterior area. The unaesthetic appearance normally prompts removal (Fig. 21.10).

Distomolars are supernumerary molar teeth that occur distal to the third molars as shown in Figure 21.11. They are the second most common supernumerary teeth. They typically show the normal crown anatomy of a molar but are slightly smaller in overall dimensions. The mandibular premolar area is another common site of preference for the development of supernumerary teeth (Fig. 21.12). Supernumerary teeth are rare in the deciduous dentition, but when it does occur, the lateral incisor is the site most affected.

Increased Number of Teeth Associated with Syndromes

In most cases of hyperdontia, the formation of extra teeth is not associated with a readily identifiable genetic disease. However, as in anodontia, some genetically inherited conditions are consistently connected with hyperdontia, and the presence of supernumerary teeth can be so dramatic that it becomes the clinical characteristic that allows initial recognition of the associated syndrome.

Cleidocranial Dysplasia (Dysostosis). Previously called "cleidocranial dysostosis," cleidocranial dysplasia is now the

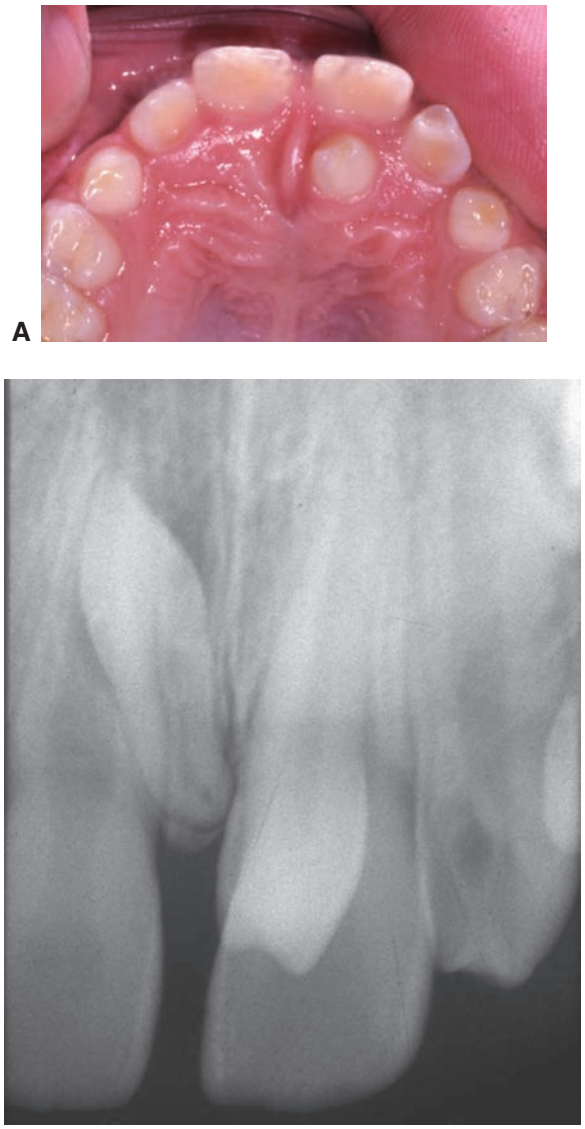


FIGURE 21.10. Hyperdontia. **A**. A mesiodens has erupted palatal to the left maxillary central incisor tooth. **B**. A radiograph of the area seen clinically in **A** reveals a second, impacted mesiodens present upside down in the maxilla behind the right maxillary central incisor.

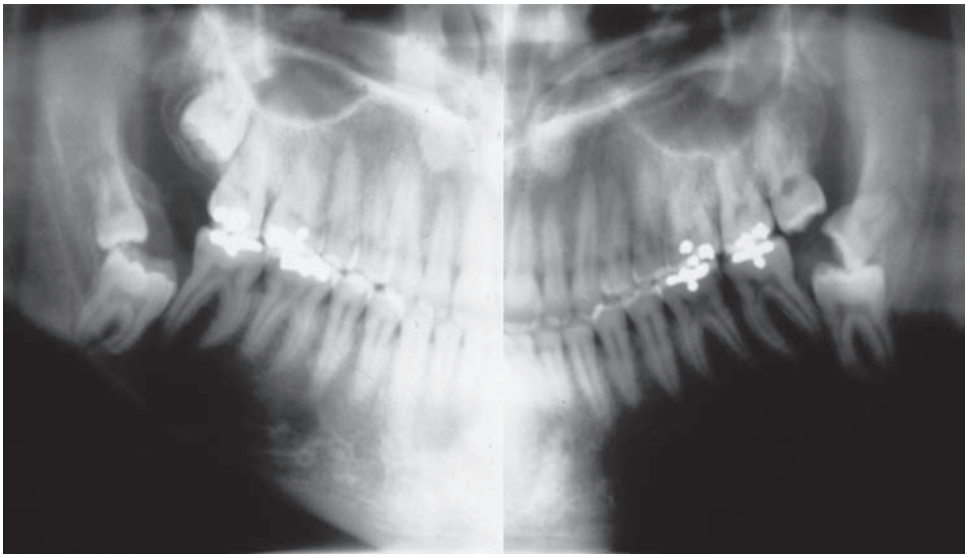


FIGURE 21.11. Hyperdontia. Bilateral mandibular distomolars are present.

preferred terminology for this genetic disease. In most cases, affected individuals have an affected parent, indicating that the disease is transmitted as an autosomal dominant trait. In up to 40% of cases though, neither parent of the affected individual shows evidence of the disease, suggesting that a good proportion of cases arise as new mutations in the individual patient's genetic makeup. The disease produces a wide array of clinical features that assist in its identification. While the name of the disease seems to indicate that only the clavicle (*cleido*) and the skull (*cranial*) are affected, membranous bones throughout the skeleton appear to be involved. Affected individuals are typically short in stature with the average height of males and females reportedly 5′2″ and 4′10″, respectively. The oral findings are truly remarkable and produce a **pathognomonic** (clearly recognizable) radiographic appearance that is diagnostic for this condition. The midface area is often deficient, resulting in the appearance of overdevelopment of the lower jaw. The palate is often cleft. The most striking radiographic feature, however, is the presence of multiple impacted supernumerary teeth (Fig. 21.13). Patients routinely have 10 or more supernumerary teeth. The sheer number of teeth present within the jaws produces overcrowding that prevents eruption of both the regular adult dentition and the supernumerary teeth. Moreover, the teeth of patients with cleidocranial dysplasia lack deposition of cellular cementum on the roots, further hindering eruption. Due to this lack of eruption of the permanent teeth, deciduous teeth are retained well past the normal expected age of exfoliation.

FIGURE 21.12. Hyperdontia. A supernumerary mandibular premolar has erupted lingual to the normally positioned premolars in the left mandible. (Photo is taken in intraoral mirror.)

Gardner Syndrome. Gardner syndrome is a disease process that may present with head and neck manifestations, including hyperdontia, which is vitally important for the dental health care practitioner to recognize. While the degree of hyperdontia is not as spectacular as is seen in cleidocranial dysplasia, the presence of supernumerary teeth in concert with other characteristic features seen on dental panoramic radiographs may be enough to alert the vigilant observer to the presence of the disease (Fig. 21.14).

Gardner syndrome is a genetic disease that is transmitted as an autosomal dominant trait. The disease is highly **penetrant**, meaning that patients who inherit the defective gene from a parent will normally show many, if not all of, the characteristic features. The dental findings include multiple supernumerary teeth that are often impacted. Multiple odontomas may be seen as well. Other features of the disease include multiple epidermoid cysts of the skin, which are particularly common in the neck, and desmoid tumors found principally in the abdominal area but occasionally found in other soft tissue sites as well. Multiple osteomas involving the skull, face, and jaws is a distinguishing feature. The angle and ramus areas of the mandible are often involved, producing irregularly dense radiopaque masses on dental panoramic films that are not seen in any other disease process. This feature in particular heralds the presence of Gardner syndrome. The primary characteristic feature of Gardner syndrome, and the feature that makes its recognition so important, is the presence of numerous polyps in the

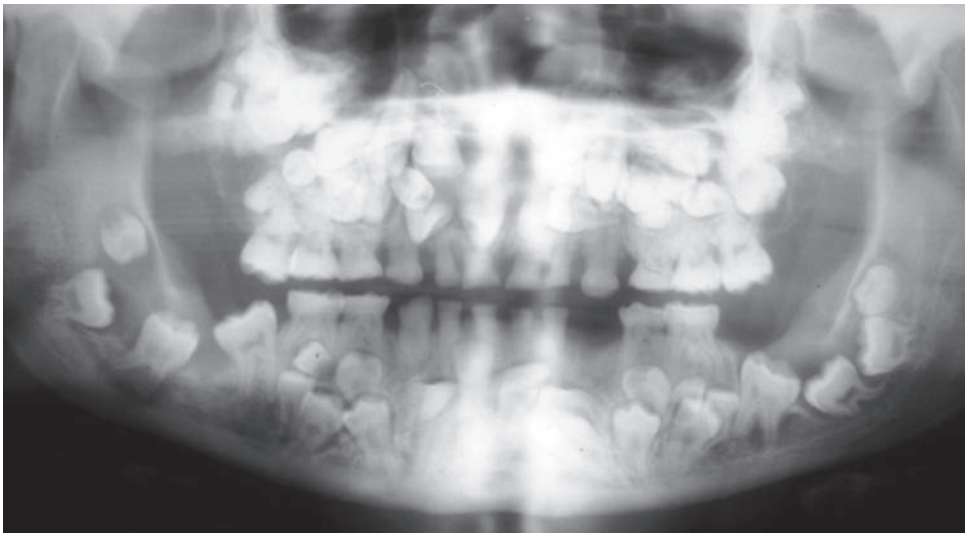


FIGURE 21.13. Cleidocranial dysplasia. Multiple impacted supernumerary teeth are a pathognomonic finding. As many as 50 teeth may be present. (Photograph courtesy of Dr. William Binnie.)

large intestine and rectum. In aggregate, these polyps have a virtual 100% incidence of eventual transformation to cancer. There is such a strong association of the development of cancer in these patients that individuals diagnosed with the syndrome often undergo **prophylactic** removal of the colon, sometimes in the very early adult years. Recognition of the characteristic head and neck manifestations is so important because development of the head and neck abnormalities typically precedes development of the colonic polyps. Early diagnosis of the syndrome, coupled with early bowel removal, may therefore be a life-saving procedure.

Other Syndromes Exhibiting Hyperdontia. The formation of supernumerary teeth is a characteristic associated with a number of other genetically linked syndromes. At least 16 additional syndromes other than cleidocranial dysplasia and Gardner syndrome are currently included on the list. In most of these syndromes, the hyperdontia is not a prominent component, with only an occasional supernumerary tooth being found. Therefore, the presence of supernumerary teeth will not usually allow ready recognition of the disease process as it does in cleidocranial dysplasia and Gardner syndrome. Paradoxically, many of the genetic diseases that are associated with supernumerary teeth also show up on the list of genetic syndromes that can produce a decreased number of teeth. These include Crouzon syndrome, Down syndrome, Ehlers-Danlos syndrome, Hallermann-Streiff syndrome, orofaciodigital (type I) syndrome, and Sturge-Weber syndrome.

Alterations in the Size of Teeth

Decreased Size of Teeth/Microdontia

Microdontia is a decrease in the size of the teeth relative to what is considered the normal range for each class of tooth. Microdontia may be generalized, affecting the entire dentition, or it may be localized, affecting only one or a few teeth.

A true generalized microdontia is relatively rare. Most cases of true generalized microdontia are associated with pituitary dwarfs. These individuals either lack growth hormone production by the pituitary gland or their tissues do not respond appropriately to the presence of growth hormone. Since growth hormone is responsible for growth of all the

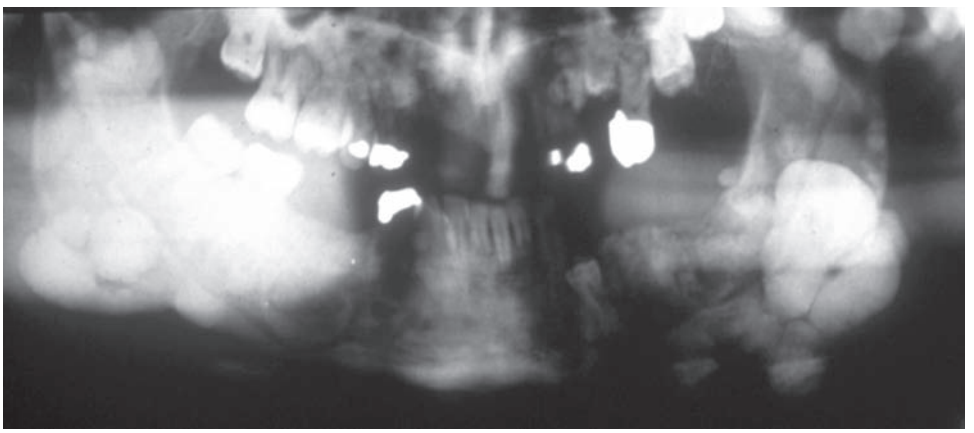


FIGURE 21.14. Gardner syndrome. The panoramic radiograph shows large osteomas involving the angle and ramus areas of the mandible bilaterally, a diagnostic feature. Several supernumerary premolar teeth are also seen.

tissues of the body, these individuals are well proportioned but are smaller in every respect, including the teeth. Patients with Down syndrome have also been reported to have a true generalized microdontia in some instances.

Perhaps more common than a true generalized microdontia is relative generalized microdontia. In this situation, the teeth are on the small end of the normal size range, but the bone of the jaw is larger than normal. The teeth therefore appear small when viewed in the context of the size of the jaw, but actual measurements show them to be within the normal range.

Localized microdontia is seen far more commonly. In general, the teeth usually affected by localized microdontia are the same as the teeth most commonly missing in cases of hypodontia. Thus, third molars are most often affected, with maxillary lateral incisors being the second most often involved. When the lateral incisor is affected, it often assumes a peg-shaped crown form. These teeth are sometimes referred to as peg laterals (Fig. 21.15). Bilateral symmetry is often noted in localized microdontia.

FIGURE 21.15. Microdontia. **A.** The lateral incisors are involved bilaterally. Note the conical crown form. These teeth are sometimes referred to as peg lateral incisors. **B.** A mandibular third molar is severely reduced in size. (Photograph courtesy of Dr. John Wright.)

Increased Size of Teeth/Macrodontia

Macrodontia is an increase in the size of the teeth relative to what is considered the normal range for each class of tooth. As with microdontia, macrodontia may be generalized, affecting the entire dentition, or it may be localized, affecting only one or a few teeth.

True generalized macrodontia is unusual. Most cases are associated with pituitary giantism. These patients typically have a tumor of the pituitary gland that secretes excess quantities of growth hormone. The excess growth hormone stimulates overgrowth of all tissues in the body. These individuals are well proportioned but larger in every respect, including the teeth. Pituitary giants typically are extraordinarily tall, with many attaining a height of more than 8 feet.

Relative generalized macrodontia is also known to occur. As with relative generalized microdontia, this is due to a lack of coordination between tooth size and jaw size, with the jaw being smaller than average, while the teeth are on the large end of the spectrum of normal size. The illusion, then, is that all the teeth are excessively large.

Localized macrodontia is relatively rare. Only isolated teeth tend to be affected, and usually only a single tooth is involved. However, bilateral symmetry may be seen with this condition (Fig. 21.16).

A developmental anomaly of unknown etiology that may produce localized macrodontia affecting many teeth is hemifacial hyperplasia. In this disease, one-half of the face enlarges relative to the opposite side, and in many cases, the enlargement is present at birth. The growth on the enlarged side keeps pace with the growth on the unaffected side, resulting in continual facial asymmetry that is evident throughout the childhood years and into adult life. Typically, the canine, premolar, and molar teeth on the affected side in both the maxilla and the mandible will show evidence of macrodontia. The affected teeth may also erupt ahead of the corresponding teeth on the unaffected side.

Macrodontia may be simulated by other dental anomalies. Close clinical observation, along with radiographic evaluation, will usually allow accurate diagnosis. Fusion of teeth, particularly when the fusion occurs between a normal tooth and a supernumerary tooth, is the most likely anomaly to be misinterpreted as macrodontia. Gemination may produce similar confusion if minimal separation of the crowns of the geminated tooth is present.

Alterations in the Shape (Morphology) of Teeth

There are a variety of abnormalities affecting the teeth that produce recognizable clinical and/or radiographic changes without affecting the structural integrity or hardness of the tooth. These are referred to as changes in the morphology of the teeth. Abnormalities affecting the crown of the tooth are easily recognized because of the unusual clinical appearance of the crown as it is viewed in the oral cavity. Abnormalities affecting the roots of the teeth generally require radiographic analysis for recognition.

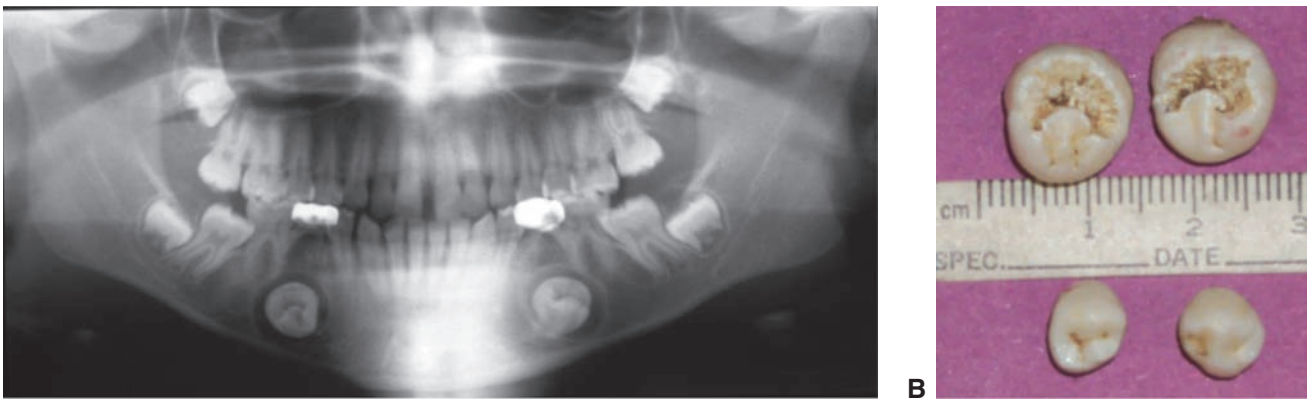


FIGURE 21.16. Macrodontia. **A.** Panoramic radiograph shows impacted macrodont premolars. Compare macrodont size with size of normal erupted premolars. **B.** Extracted specimens from **A** allow measurable comparison of size of macrodonts compared to normal mandibular premolar teeth.

Abnormalities Affecting the Crowns of Teeth

Shovel-Shaped Incisors. Shovel-shaping of the incisor teeth is an aberration that is of no clinical significance and can go completely unrecognized without adverse consequences. The affected teeth show markedly thickened mesial and distal marginal ridges that extend apically from the incisal edge, eventually blending into the lingual surface. When the tooth is viewed from above the incisal edge, the lingual surface resembles the blade of a shovel, accounting for the descriptive name applied to this morphologic variation. Characteristic shovel-shaping is depicted in Figure 21.17. The radiographic appearance of the involved teeth is typically unremarkable. Patients with shovel-shaping of the incisor teeth may have other associated abnormalities of the teeth. Dens invaginatus and dens evaginatus (see below) are the most commonly reported accompanying abnormalities. The importance of shovel-shaped incisors lies only in its anthropologic implications. Shovel-shaped incisors are seen with increased frequency in East Asian populations, Siberian Eskimos, Alaskan Eskimos, and Native Americans. This distribution of populations affected with shovel-shaped incisors is sometimes cited as evidence of an ancient land bridge spanning the current Bering Sea that allowed Asian populations to migrate and populate the Western hemisphere.

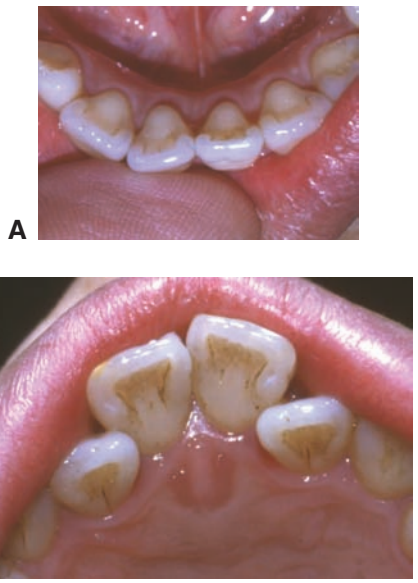


FIGURE 21.17. Shovel-shaped incisors. **A.** The mandibular incisors show prominent mesial and distal marginal ridges, producing the characteristic shovel shape on the lingual surface. **B.** The maxillary incisor teeth in the same patient.

Accessory Cusps. Accessory cusps are supplementary cusps that alter the expected surface anatomy of a tooth. They are typically nonfunctional and can affect any tooth.

Cusp of Carabelli. The cusp of Carabelli is the best known and most common of the accessory cusps. In fact, it is so common that it is considered part of the normal anatomy of the maxillary first molar tooth in certain populations. It is found as an elevation on the palatal surface of the mesiolingual cusp. It may be very small and rudimentary or it may be prominent enough to produce a groove in the lingual surface of the mesiolingual cusp. When a groove is present, it may predispose the area to the development of a carious lesion. The cusp of Carabelli is also seen frequently on the deciduous second molar tooth, and its presence in the deciduous dentition is a good indication that it will also be seen in the permanent dentition. It is far less frequently found on permanent second and third molar teeth. The prevalence of the cusp of Carabelli is highest in whites and is rarely reported in Asian populations. Some studies report that it is more common in male patients. The cusp of Carabelli is not normally visualized on radiographic examination.

Talon Cusp. The talon cusp is an accessory cusp that arises from the cingulum area of an incisor or canine tooth. It is markedly elongated to the point that the tip of the elongated cusp may approach the level of the incisal edge of the tooth. The elongated cusp is normally fused to the lingual surface of the affected tooth, producing a three-pronged appearance (Fig. 21.18A). A groove may be present at the points where the accessory cusp fuses with the lingual surface and may dispose the area to development of a

carious lesion. This accessory cusp is termed a talon cusp because, when viewed from the incisal aspect, the prominent three-pronged, T-shaped pattern evident on the lingual surface roughly resembles the talon shape seen in the claws of birds of prey. The talon cusp most often affects a single tooth, but bilateral involvement sometimes occurs. The elongated cusp usually contains a pulpal extension, and adjustment of the height of the accessory cusp may result in pulp exposure, necessitating endodontic therapy. Occasionally, the length of a talon cusp may interfere with occlusion, blocking the normal overbite relationship of the anterior teeth. Reduction of the talon cusp is necessary in this circumstance. On rare occasions, a talon cusp has been seen to arise from the facial surface of a tooth rather than the lingual side. Because this cusp is quite prominent, it usually produces a characteristic radiographic appearance, with the additional cusp being easily visualized on periapical radiographs as depicted in Figure 21.18B.

Doak's Cusp. Doak's cusp is an accessory cusp that is found on the facial surface of maxillary molar teeth

A

B

FIGURE 21.18. Talon cusp. **A.** The right maxillary lateral incisor shows a markedly elongated cingulum cusp, producing the talon-like architecture when viewed from the incisal. **B.** Radiographic features of the talon cusp seen in **A**.

FIGURE 21.19. Doak's cusp. An accessory cusp is present on the mesiobuccal cusp of the maxillary second molar tooth.

(Fig. 21.19). As with most accessory cusps, an increased incidence of caries may be seen in the groove that often is present at the point where the accessory cusp fuses with the facial surface. A pulp horn normally extends into the cuspal elevation, limiting the ability to reduce the cusp height for restorative or aesthetic purposes. It is often not visualized on radiographic evaluation.

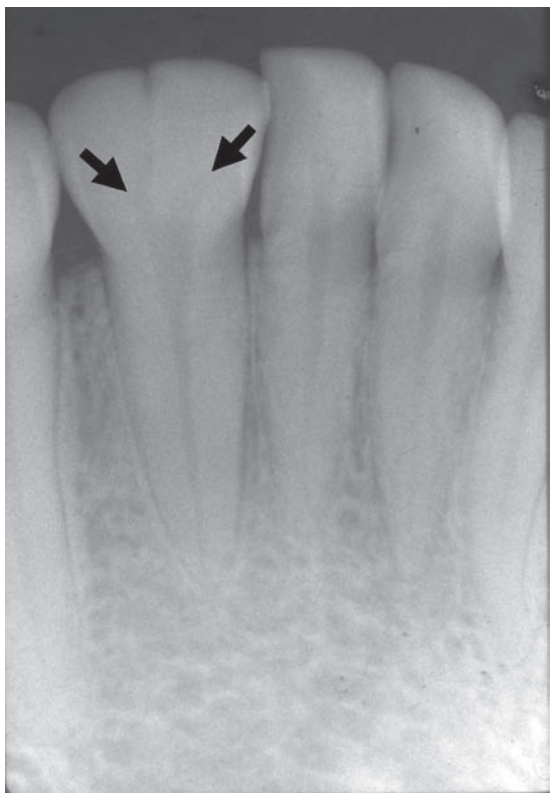
Dens Evaginatus. "Dens evaginatus" is a term used to describe an anomalous cusp that emanates from the central groove on the occlusal surface of posterior teeth as depicted in Figure 21.20. The premolar teeth are affected most often, with molar teeth being only occasionally involved. Mandibular teeth are affected with greater regularity than maxillary teeth. Bilateral involvement is generally the rule. Dens evaginatus is seen with increased frequency in Asians. The accessory cusp may interfere with normal occlusion if it is of sufficient size. It normally contains a pulpal extension, and adjustment of the occlusion requires caution to prevent pulp exposure. It is often difficult to identify this cusp on periapical or panoramic radiographs unless it is first noticed clinically. Shovel-shaping of the incisor teeth is a common accompanying feature.

Gemination. Gemination is defined as the attempt by a single tooth germ to produce two teeth. In the past, it was also referred to as "twinning" by some researchers. On clinical observation, if the visible crowns are counted, a supernumerary tooth may seem to be present, fused to the adjacent normal tooth. However, radiographic evaluation reveals the diagnostic features. The root canal system, which appears essentially normal within the root area, splits as it ascends toward the crown. Thus, the two crowns appear to

FIGURE 21.20. Dens evaginatus. An accessory cusp emanates from the central groove in the occlusal table of a maxillary premolar.

arise from a single root, having separate pulp chambers but sharing the same root canal (Fig. 21.21). In many instances, both the root and the root canal space may appear slightly enlarged relative to the adjacent unaffected teeth. The maxillary incisors are the most commonly affected teeth. The incidence of gemination decreases dramatically from anterior to posterior, with gemination involving the molars being basically nonexistent. In the deciduous dentition, the mandibular incisors are more commonly involved than the maxillary. There does appear to be a hereditary tendency in the incidence of gemination.

A



B

FIGURE 21.21. Gemination. **A.** The right mandibular lateral incisor appears much larger than the other mandibular incisors and has a prominent groove in the incisal edge that blends into the facial surface. **B.** The radiograph of the right mandibular lateral incisor shows a single root with an attempt to form two crowns. Note the splitting of the pulp in the coronal area.

Fusion. Fusion occurs when tooth buds develop in such close proximity that contact occurs as the dentinal matrix is formed and calcified. The crowns of the two teeth are found to be inextricably joined by the shared dentin. On clinical observation, when counting the number of visible crowns, a tooth appears to be missing. Again, radiographic evaluation reveals the diagnostic features. Two complete root complexes, each containing a separate root canal system, are present. The two roots merge as they ascend occlusally, producing a single composite crown. Typically the root canal systems remain separate within the fused crown structure. Because this abnormality results from the linking of two adjacent normal teeth, the composite crown produced may appear larger than normal and, before radiographic examination, may initially be interpreted as a macrodont (Fig. 21.22). Like gemination, fusion is seen most commonly in the anterior regions of the jaws. In contrast to gemination, however, it is more commonly found in the deciduous dentition than in the permanent teeth.

Congenital Syphilis. Abnormalities in the morphology of the teeth produced by the **venereal** disease syphilis are decidedly rare in the modern era. In the past, particularly prior to the development of antibiotics, these abnormalities were seen with much greater frequency. The tooth abnormalities produced by syphilis are seen only when the infection is passed from the infected pregnant mother to the fetus. This is believed to occur following 4 months in utero. The causative organisms, *Treponema pallidum*,

FIGURE 21.22. Fusion. The mandibular central and lateral incisors are fused. Note two separate root structures with fusion of the crowns of the teeth only.

cross the placental barrier at that time. These spirochetes have an affinity for the developing tooth germs and produce distinctive alterations in the shape of the teeth that are developing in the neonatal period. Incisor and first permanent molar teeth are typically affected. In the incisor teeth, the organisms are believed to produce loss of the developing middle mammelon of the incisal edge. At eruption, the tooth is seen to have marked narrowing of the width of the incisal edge, producing a screwdriver shape. The middle portion of the incisal edge is often notched. These teeth are referred to as "Hutchinson incisors" (Fig. 21.23A).

The first permanent molar also shows severe alteration of the occlusal anatomy of the tooth when it erupts, with the normal five cusp architecture being replaced by an excessive number of small supernumerary cusps on a constricted occlusal table. Because of this "knobby" occlusal pattern, these teeth are referred to as "mulberry molars" (Fig. 21.23B).

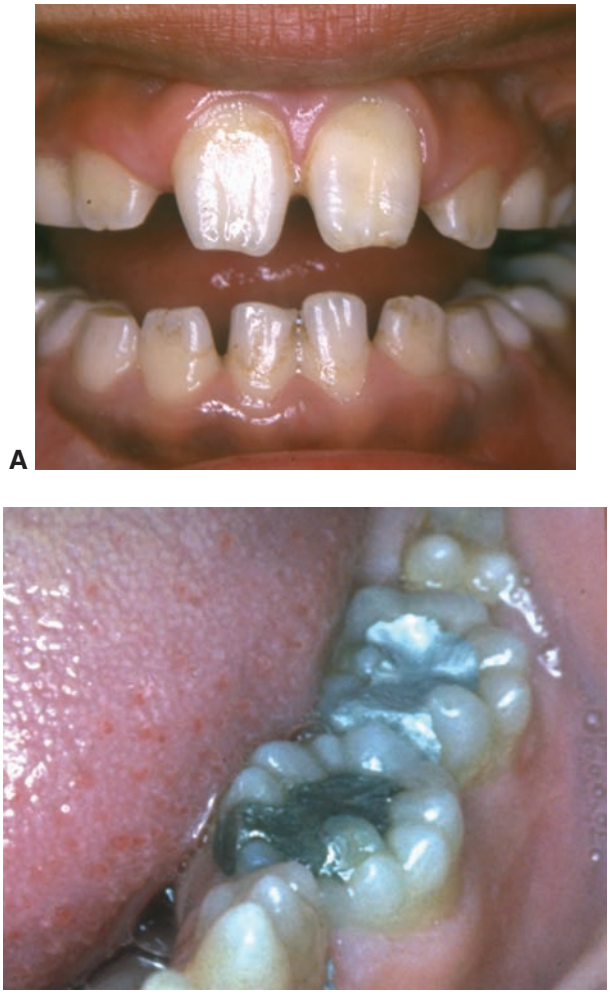


FIGURE 21.23. Syphilis. **A.** The incisor teeth show narrowing of the width of the incisal edge with a screwdriver-like shape. This feature is termed Hutchinson incisors. **B.** The molar teeth, despite having been restored, show multiple irregularly distributed small cusps. This feature is termed "mulberry molars." (Both photographs courtesy of Dr. William Binnie.)

The infected child, born into the second stage of syphilitic infection, shows multiple other anomalies that facilitate recognition of the disease. In addition to the tooth abnormalities, deafness due to loss of function of the eighth cranial nerve and opacification of the cornea with loss of eyesight are common manifestations. This constellation of findings is referred to as "Hutchinson triad."

Lobodontia. Lobodontia is a genetically transmitted disease that is named for the distinctive alteration of crown morphology that it produces. Studies of several afflicted **kindreds** (families) suggest that it is transmitted as an autosomal dominant trait. The teeth appear to be the only structures affected, with no associated abnormalities reported in other body areas or systems. Lobodontia was originally described by Keene and Dahlberg in 1973. They noted multiple anomalies of the dentition that they felt resembled the teeth of a wolf (*lobo*, wolf). Other authors have suggested that the affected teeth resemble those of dogs. The most prominent change seen in the crowns of affected teeth is the elongation of some of the cusp tips, while other cusps are reduced in height. The buccal cusps are more commonly elongated, although the molars typically show multiple affected cusps. The anterior teeth may also show elongation of the cingulum area, and a pit or invagination in the cingulum area often accompanies the elongated cingulum cusp. The elongated cusp tips are often very pointed and almost fang-like in appearance. Generally, the teeth are smaller than average. All of the teeth may be affected, or limited involvement of only some teeth may be seen. On radiographic evaluation, additional characteristic features may be noted. The roots of all teeth tend to be narrowed. The molar teeth, rather than being multirooted, have a single, tapering root that also appears narrower than normal and contains a single root canal space. This creates the illusion of an overly large, bulbous crown on top of the tapering root that produces an "ice cream cone" appearance.

Treatment of patients with lobodontia may prove difficult, although the problems are not insurmountable. The elongated cusp tips may contain a correspondingly elongated pulp horn, and reduction of the elongated cusps for aesthetic purposes, particularly in the anterior region, may result in pulp exposure and the need for endodontic therapy. Likewise, intracoronal preparations risk pulp exposure. Periapical radiolucent lesions may develop due to the invaginations that are commonly seen in the cingulum area of the anterior teeth. The conical root form of the molar teeth often makes these patients poor candidates for fixed bridge abutments should prosthodontic replacement of teeth become necessary. Otherwise, treatment is routine and is often directed at improvement of the aesthetics.

Globodontia. Globodontia may be confused with lobodontia because of the name similarity, but it is a separate condition. Unlike lobodontia, which affects only the teeth, globodontia is a component of the oculo-oto-dental syndrome, a genetic disease process that produces distinctive abnormalities of other body systems that are consistently

present in the affected patients. Oculo-oto-dental syndrome is transmitted as an autosomal dominant disease, and it has been definitively mapped to a specific gene found on chromosome 20 (20q13.1). The findings other than abnormalities of the shape of the teeth that are associated with oculo-oto-dental syndrome include **colobomas** of the iris and retina (absence or defect of some portion of the eye tissues) and progressive sensorineural deafness for high-frequency sounds.

The tooth abnormality associated with oculo-oto-dental syndrome consists of bizarre, greatly enlarged teeth (macrodontia). Interestingly, the condition appears to affect all of the teeth except the incisors. The crowns are decidedly rounded, bulbous, or globe-like, accounting for the descriptive name used for this tooth abnormality. The typical fissured anatomy of the occlusal table of the posterior teeth is nearly obliterated, with the occlusal surface having a convex dome-shaped appearance. On radiographic examination, the molar teeth show taurodontism (discussed below). In addition, the pulps of the involved teeth appear larger than usual. Congenitally missing teeth may also be associated with this syndrome.

Abnormalities Affecting the Roots of Teeth

Abnormalities affecting the roots of the teeth can be grouped into two categories: (1) abnormalities produced by alterations in Hertwig epithelial root sheath, the structure that directs the growth and form of the root, and (2) abnormalities produced by overproduction of cementum on the surface of the root. Abnormalities affecting the roots are generally not evident on clinical examination; however, they are detected in the subsequent dental radiographs.

Accessory Roots (Supernumerary Roots). Accessory roots are a fairly commonly observed irregularity of root form that is sometimes referred to as "supernumerary roots." It is believed to be produced by overproliferation of a segment of Hertwig epithelial root sheath, resulting in extraneous root formation as shown in Figure 21.24. The molar teeth are the most commonly affected, but it can involve any tooth in either arch. The incidence varies among different races. Accessory roots are an inconsequential finding in most cases. It becomes significant only should endodontic therapy or extraction of the involved tooth become necessary. Since the accessory root is often smaller and thinner than the adjacent roots, locating and obturating the root canal space during endodontic therapy may be more difficult. The small, thin nature of the accessory root also makes it more prone to accidental fracture during extraction of the tooth, producing an increased incidence of complications during such procedures. Because of the reduction in size and overlap with the other roots of the tooth, accessory roots may not be easily visualized on radiographs.

FIGURE 21.24. Accessory roots. Maxillary molar teeth showing four roots rather than the customary three.

FIGURE 21.25. Dilaceration. A maxillary lateral incisor showing excessive curvature of the root. There was a history of trauma to the area as a very young child.

Dilaceration. Dilaceration is defined as a markedly abnormal curvature in the shape of the root (Fig. 21.25). It can affect any tooth and can be seen at any level of the root. It is believed to be caused most often by trauma to the area of the developing tooth that slightly displaces the position of the already calcified portion of the tooth, without affecting Hertwig root sheath. Pathologic conditions occurring adjacent to a developing tooth have also reportedly produced dilacerations. Teeth exhibiting dilacerations may show a delay or failure of eruption that requires dental intervention. Otherwise, dilaceration is clinically insignificant in most instances. As with accessory roots, however, significant problems can be encountered should endodontic therapy or extraction be necessary in a tooth with a dilacerated root. It has also been suggested that teeth with dilacerated roots may be less desirable for use as an abutment tooth for a fixed bridge or less amenable to orthodontic movement.

Enamel Pearl. Enamel pearls are abnormalities of root formation that are of particular importance for dental hygienists and periodontists. Enamel pearls are likely produced by an abnormality in Hertwig epithelial root sheath in which an area of **stellate reticulum** (the middle layer of enamel organ) is retained between the two layers of epithelium that normally comprise the root sheath. The presence of the stellate reticulum allows differentiation of the root sheath cells into ameloblasts, leading to the formation of a small area of enamel on the external root surface. The enamel typically forms as a small, rounded, nodular elevation that produces an area of increased radiopacity on the radiograph. In many

FIGURE 21.26. Enamel pearl. A small dome-shaped nodule is present firmly attached to the root surface. Note the *bright white* surface of the nodule has the same color and translucency as the enamel on the crown.

instances, a dentin core exists within the nodular elevation, and a pulp horn may also be present. The enamel pearl is most commonly found in the furcation area of molar teeth, but it can occur anywhere along the root surface down to the midroot level. It is rarely encountered in the lower one-half of the root. Maxillary teeth are involved more often than mandibular teeth, and Asian populations appear to be affected more commonly than other races. When the enamel pearl occurs in the furcation area, it may disrupt the normal epithelial attachment apparatus in the area, producing a periodontal defect. Periodontal probing of the area reveals an excrescence on the root surface in the area (Fig. 21.26), and the radiograph shows an area of increased opacity, all of which often add up to the mistaken impression that the periodontal defect is due to calculus deposition. Scaling may be performed in an attempt to remove the adherent material, which is solidly fused to the root surface and cannot be dislodged. Repeated attempts at removal with ever-increasing application of force to the scaler may eventually result in breakage of the instrument. Once recognized as an enamel pearl, treatment may prove problematic when it is present in the furcation area. Surgical removal may be deemed necessary to correct the periodontal problem but may result in pulp exposure if a pulp horn is present within the core of the enamel pearl. In such situations, endodontic therapy may become necessary.

Taurodontism. Taurodonts are believed to occur because of a failure of proliferation of that portion of Hertwig epithelial root sheath that is responsible for development of the morphologic form of the roots. Since this occurs only in multirooted teeth, taurodontism is seen almost exclusively in molar teeth. They are called taurodonts because they show some resemblance to the teeth seen in bulls. The body of the tooth is enlarged at the expense of the roots. The typical cervical constriction in the cementoenamel junction area is reduced or may be entirely absent. This gives the superior portion of the tooth a rectangular appearance on radiographic appraisal. The pulp chamber is enlarged and appears to penetrate more deeply into the root area. The roots are shortened, often markedly so. Three types of taurodont teeth are described. Hypotaurodonts show only slight shortening of the roots with a mild increase in size of the pulp chamber, and the changes may be subtle enough that the condition goes unrecognized. Mesotaurodonts show obvious shortening of the roots with a corresponding increase in the size of the pulp chamber, and hypertaurodonts show severe root shortening. Taurodontism primarily affects the permanent teeth. While it may be unilateral in occurrence, it is often seen in a bilaterally symmetrical pattern (Fig. 21.27). Taurodontism has been identified as a component of some genetically based syndromes. Down syndrome is the disease most often noted in association with taurodontism.

Concrescence. Concrescence is a rare abnormality that is similar to fusion. In contrast to fusion, however, the union of the affected teeth is not via the dentin but due to overproduction of cementum on the root surface of two or more teeth that are positioned in close proximity as depicted in Figure 21.28. The teeth therefore tend to be joined in the apical region and the abnormality is discovered on radiographs. In fusion, the crowns tend to be conjoined rather than the roots, allowing rapid recognition and delineation of the two processes. Concrescence occurs most frequently in the posterior regions of the jaws, and the maxilla is affected more often than the mandible. Concrescence normally has little clinical significance unless extraction of the involved teeth becomes necessary.

Hypercementosis. Hypercementosis is defined as excessive production of cementum on the root surface. It may involve only a single tooth, it may affect multiple teeth in the same area, or it may be seen in multiple quadrants. When it is seen in multiple quadrants, a metabolic abnormality may be identifiable as the underlying cause. Hypercementosis, if particularly excessive, could eventuate in concrescence, particularly if multiple adjacent teeth are producing excessive amounts of cementum. Clustering of cases in some family groups suggests a hereditary influence in the development of hypercementosis. The apical one-third of the root is affected, and the process does not appear to involve other areas of the root without involvement of the apical area. The incidence of hypercementosis increases with aging, and children are rarely affected. The premolar teeth are statistically the most commonly involved. Diagnosis is made via dental radiographs. The root end of the tooth appears enlarged and often is bulbous at the tip. Characteristically, a thin radiolucent rim separates the affected area from the surrounding alveolar bone. This lucent halo blends into the normal periodontal membrane space in those areas of the tooth unaffected by the hypercementosis, indicating that the periodontal membrane is maintained intact around the area of excessive cementum production (Fig. 21.29).

Hypercementosis has been positively associated with a number of disease processes that show alterations in bone metabolism. Paget disease of bone, acromegaly, and pituitary giantism are included in this group. Paget disease in particular has a very strong association, to the point that patients presenting with multiple teeth

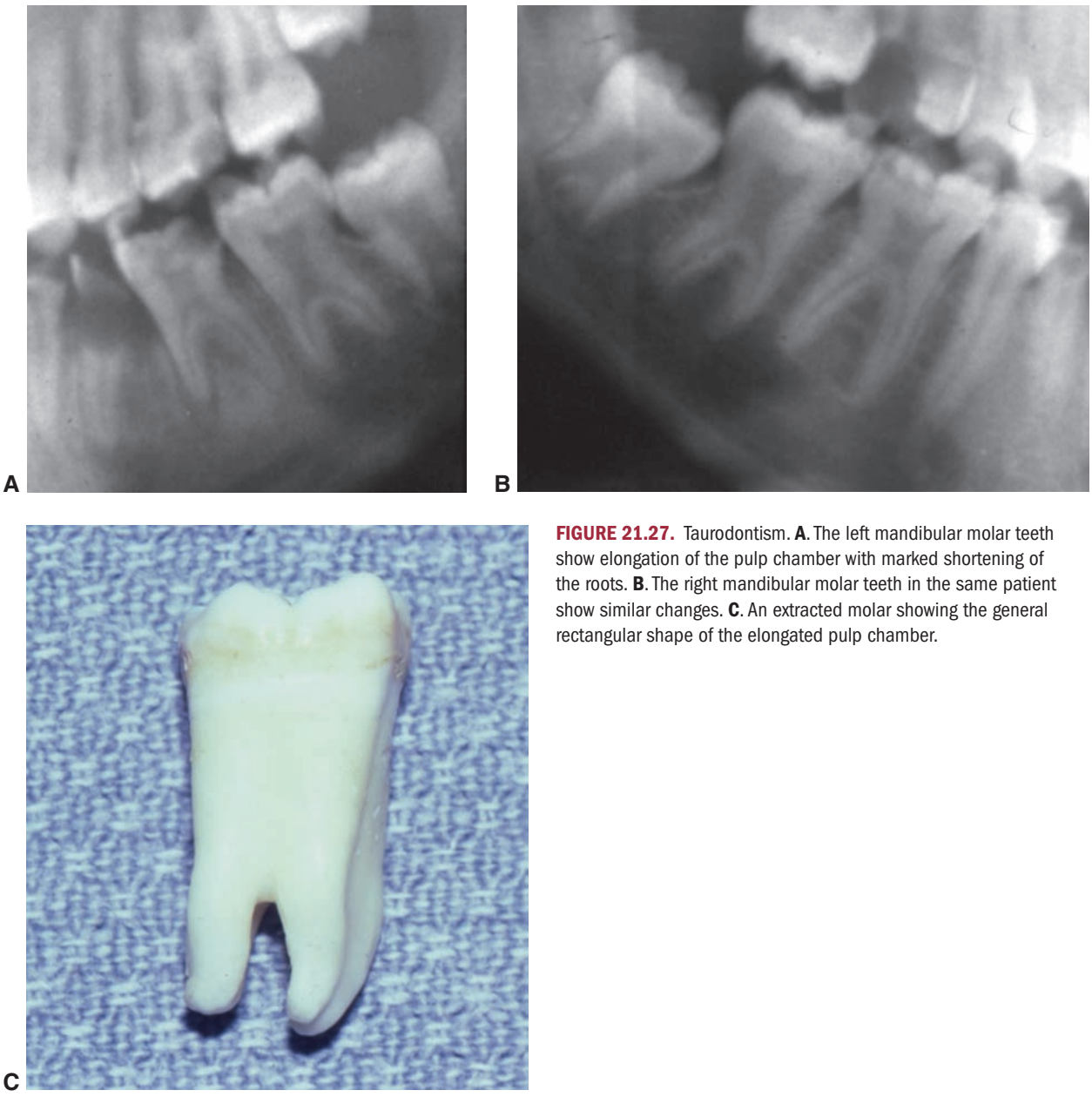


FIGURE 21.27. Taurodontism. **A.** The left mandibular molar teeth show elongation of the pulp chamber with marked shortening of the roots. **B.** The right mandibular molar teeth in the same patient show similar changes. **C.** An extracted molar showing the general rectangular shape of the elongated pulp chamber.

showing hypercementosis should be sent for serum alkaline phosphatase analysis to rule out Paget disease. Inflammatory stimulation of the cementum-producing cells of the periodontal ligament may also result in hypercementosis. This is evidenced by the presence of hypercementosis, albeit mild, in a large number of cases of long-standing periapical granuloma. Teeth found to be in traumatic occlusion and, ironically, nonfunctional teeth (teeth without an opposing tooth in occlusion) may also show hypercementosis. Hypercementosis is of limited clinical significance and does not compromise normal function in most instances. If extraction becomes necessary, difficulty may ensue, and surgical extraction may be necessary if the degree of hypercementosis is substantial. The dental hygienist must have a good clinical understanding of the features of hypercementosis to distinguish it from cementoblastoma, a true neoplastic proliferation of cementum. In hypercementosis, the root maintains its general form, but it is enlarged, and the root tip area can be visualized in the bone. In cementoblastoma, the proliferation of cementum obscures the form of the root, which seems to "disappear" into the radiopaque lesion that surrounds the apex area. Thus, the root tip of the involved tooth is not clearly visualized in cementoblastoma.

Alterations in the Structure of Teeth

Defects in the function of the cells that are responsible for the development and calcification of the teeth can result in pathologic conditions. These abnormalities generally affect

FIGURE 21.28. Concrescence. The teeth are fused by the cementum of the roots.

the structural integrity of the tooth, the hardness of the calcified components of tooth structure, or the normal anatomic arrangement and structural interrelationships of the different layers of the tooth. The affected teeth may appear entirely normal in the shape of the crown and root when viewed clinically in the oral cavity or on radiographic examination. In some instances, however, the alteration in the structure of the calcified components produces clinical and/or radiographic changes that can be visualized as well. Most of the disease processes included in this category have a genetic basis.

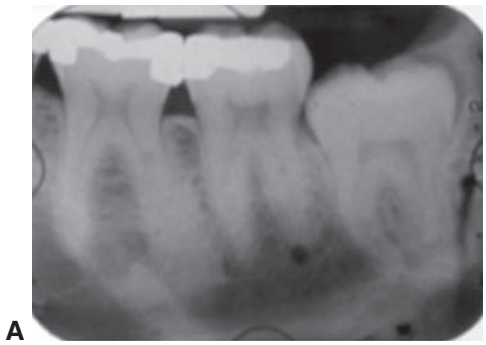


FIGURE 21.29. Hypercementosis. **A.** There is a marked thickening of the cementum around the distal root of the first molar tooth. **B.** Gross specimen of extracted tooth shows thickening of the cementum at the root tip area of a molar.

Enamel Hypoplasia

Systemic illness, nutritional deficiencies, and environmental factors may produce structural defects of the enamel that are not hereditary but are still considered developmental. These defects are seen only when the associated causative disorder occurs during the period of tooth bud development and calcification.

Any systemic illness that produces a high fever may be implicated. The fever is thought to obstruct the ability of the ameloblastic cells to lay down the organic matrix that serves as the scaffold for enamel calcification. Without the organic matrix, calcification cannot subsequently occur, and the defect is produced. However, only the ameloblasts active at the time of the fever are affected. The defect appears clinically as a line or groove in the enamel surface that runs in an arc-shaped pattern roughly parallel to the incisal/occlusal line. Because the fever affects the body as a whole, all the teeth that are developing at that time are affected. Since the crowns of different teeth begin formation at separate ages, they will be at different stages of development when the fever occurs. The hypoplastic defect, therefore, is found at different levels on adjacent teeth. In general, the linear defect appears closer to the incisal/occlusal surface the further posteriorly the teeth are located, with one exception. The first permanent molars begin calcification at birth and hypoplastic defects in these teeth will be found at close to the same level of the crown as seen in the central incisor teeth. A good estimate of the age at which the illness occurred can be made by correlating the position of the defect in the enamel surface with knowledge of the timetable of tooth formation and calcification. In general, teeth with enamel hypoplasia associated with a high fever will not show significant alteration in the overall shape of the teeth.

Malnutrition may cause enamel hypoplasia as a result of the lack of the materials required by the cells to produce the enamel matrix. Alternatively, calcification of adequately formed enamel matrix may be hindered by inadequate calcium, phosphates, or other required elements in the diet. Metabolic disorders that alter the ability to absorb nutrients from the digestive system are also included in this group as causes of enamel hypoplasia. Malabsorption syndromes, liver disease, hypoparathyroid states, and renal disease are all included in this category. The enamel defects seen may vary from very mild to quite severe, depending on the degree of malnutrition present and its duration. If the degree or duration of the malnutrition is substantial, the teeth may show significant alteration of the crown shape in addition to a reduction of the enamel hardness.

Environmental factors that may produce enamel hypoplasia include an array of chemicals and medications. The teeth may be minimally or severely affected, depending on the age of the patient at initiation of therapy, the dose of the agent ingested, and its duration of usage. Changes may range from alterations of surface color or translucency

FIGURE 21.30. Enamel hypoplasia. **A.** The teeth show multiple areas of cavitation and discoloration. The cause of the hypoplasia in this patient could not be determined. **B.** Note the linear groove-like defects at differing levels in the enamel surfaces of multiple teeth. The maxillary central and lateral incisors have been previously restored for aesthetic reasons. The patient gave a history of life-threatening pneumonia with high fever at age 6 months.

to actual pitting, grooving, or cavitation (Fig. 21.30). Chemotherapeutic drugs used in the treatment of childhood malignancies are implicated in this category, since they inhibit the normal cellular mechanisms involved in matrix deposition and calcification. In some cases of enamel hypoplasia, the tooth becomes discolored in addition to exhibiting the enamel deficiencies, and it is the change in color of the tooth that leads to identification of the cause. Fluoride and tetracycline medications are the best-known causative agents and are discussed in the section on alteration of the color of teeth. Local trauma and x-radiation are also known factors in producing enamel hypoplasia.

Amelogenesis Imperfecta

In amelogenesis imperfecta, the enamel covering of the crowns of the teeth is found to be defective. The dentin and cementum are not affected. Systemic illness, malnutrition, and environmental factors play no role in its cause; instead, the condition is caused by the defective development of enamel, which has a genetic basis. Enamel development is a three-stage process that begins with enamel matrix deposition, transitioning to mineralization of the matrix, and ending with final hardening (maturation) of the enamel layers. Each stage is controlled by separate genetic mechanisms, and a defect in the genetic control at any of the three stages will produce amelogenesis imperfecta. Therefore, amelogenesis imperfecta can be subdivided into groups depending on which stage of enamel production is disrupted by the genetic defect. Numerous variations of amelogenesis imperfecta are known, and the clinical manifestations are so diverse that an entire text could be devoted to describing all of the types that might be seen. For that reason, this discussion emphasizes the general patterns seen in the main subgroups.

The largest of the subgroups is composed of those genetic defects that affect deposition of enamel matrix. Seven separate disorders have been identified in this group. These disorders show a variety of genetic inheritance patterns, with autosomal dominant, autosomal recessive, and X-linked dominant disorders all having been verified. The enamel defects seen in this category are quite varied and may present with localized or generalized pitting of the enamel surfaces, or they may simply manifest as an alteration of the surface color combined with a loss of translucency. In the most severe form of hypoplastic amelogenesis imperfecta, enamel completely fails to form. Luckily, this last type is a rare form of amelogenesis imperfecta transmitted as an autosomal recessive trait.

Hypocalcified forms of amelogenesis imperfecta affect the deposition of inorganic elements onto the organic enamel matrix. This is an uncommon form of amelogenesis imperfecta, and only two types have been identified. Both types tend to show diffuse involvement of the teeth. Autosomal dominant and autosomal recessive inheritance are seen in these two forms. Both tend to manifest clinically as a diffuse, mottled color change of the enamel.

The hypomaturation type of amelogenesis imperfecta comprises four separate genetically determined disease processes. Because the defects are limited to the final hardening of the enamel surfaces, the clinical presentation typically shows alterations in the surface color, with loss of translucency of the enamel. Pitting or cavitation is generally not present in the hypomaturation types. Diffuse involvement is generally seen, and two of the genetic patterns produce a distinctive "snow-capped" appearance in the enamel. Autosomal recessive and X-linked recessive inheritance patterns have been confirmed in two of the types. The specific genetic mode of inheritance in the remaining two types has not been definitively proven.

A final group of disorders appears to combine defects in both the deposition of enamel matrix and its maturation once the limited matrix is calcified. Two different types are known, both of which show an autosomal dominant mode of inheritance. Some evidence suggests that the two syndromes may represent two ends of the spectrum of a single disease. Color change in the enamel surface is normally seen, and pitting defects may also manifest. In addition to amelogenesis imperfecta, affected individuals show taurodontism.

Regardless of the stage at which enamel formation is disrupted, the clinical complaints of the affected patients are usually quite similar. Aesthetic concerns are often an early complaint. This is due to the presentation of multiple anterior teeth with significant color variations and/or surface defects. The specific pattern seen depends on the type of amelogenesis imperfecta that is present in the individual patient. Early loss of enamel structure often occurs, with patients noting that the enamel seems to "flake off" the tooth surface. This tends to occur easily, seemingly unprovoked by the patient. Simple chewing may result in loss of portions of the enamel. The use of ultrasonic scaling instruments may produce separation of the enamel in some of the types as well. The problem is manifested in both the deciduous and permanent dentition in most cases. Older patients also often complain that their teeth have come to appear more yellow as they age. This is the result of continual loss of the whiter, translucent enamel, allowing the underlying duller, yellow color of the dentin to be seen (Fig. 21.31).

FIGURE 21.31. Amelogenesis imperfecta. **A.** The enamel has been lost from nearly all the teeth, resulting in a prominent *yellowish* color of the dentition and more rapid attrition and abrasion. **B.** Another type of amelogenesis imperfecta shows diffuse pitting defects of the enamel surface. Note areas where the enamel has flaked off of the underlying *yellow-brown* dentin surface. (Both photographs courtesy of Dr. William Binnie.)

The radiographic pattern seen in amelogenesis imperfecta will vary depending on the specific subtype encountered, but in general, the enamel seen on the radiographs appears thinner than normal, and its density more closely approximates that of the dentin in many of the forms. Therefore, no sharp demarcation between enamel and dentin may be evident. Older patients may exhibit complete loss of evidence of enamel.

Treatment of amelogenesis imperfecta normally centers on correction of the aesthetic concerns. Some patients have sensitivity due to loss of the enamel surface with exposure of the underlying dentin.

Dens Invaginatus (Dens in Dente)

Dens invaginatus is also commonly referred to as "dens-in-dente." This accurately describes the anomaly as a tooth forming inside a tooth. It results from an abnormality in the enamel organ that produces an invagination of the enamel surface. While the actual calcified structures of the different layers of the tooth are unaffected, the customary anatomic layering of the enamel and dentin is disrupted. This causes enamel, which is normally found only on the external surface of the crown, to be found internally within the crown substructure in dens invaginatus. The invagination of the enamel surface may be minimal and difficult to recognize either clinically or radiographically. In this situation, the affected tooth looks entirely normal morphologically (Fig. 21.32A).

In other instances, the invagination is sizeable, clearly altering the normal tooth shape both on clinical observation and in the dental radiographs. Two types of dens invaginatus are recognized: the more common coronal type and the rare radicular type (Fig. 21.32B and C).

Coronal dens invaginatus is a relatively common abnormality of tooth formation, reported in one study to be present in an incredible 10% of all patients. Other studies report much lower frequencies of occurrence, usually less than 1%. The maxillary lateral incisor is the most commonly affected tooth, and maxillary teeth in general tend to be affected more often than their mandibular counterparts. Molar teeth, regardless of arch, are only rarely involved. Unilateral or bilateral involvement is possible. In occasional instances, the defect is seen in more than one tooth on the same side rather than bilaterally. In teeth that are minimally affected, the area of invagination may not be overtly obvious on clinical examination. It will sometimes be visible as a pit in the enamel surface in an area that would otherwise be expected to be entirely smooth. In maxillary incisor teeth, this is typically seen on the palatal surface in the cingulum area. The cingulum may even appear enlarged and is sometimes quite prominent. In the more severely affected forms, the cingulum area may be enlarged and elongated to the extent that a talon cusp architecture is manifest. The more severe the invagination of the enamel, the more the normal shape of the tooth is distorted. In its most severe form, the invagination will extend all the way into the root area, often perforating the lateral portion of the root and providing direct communication from the tooth surface into the

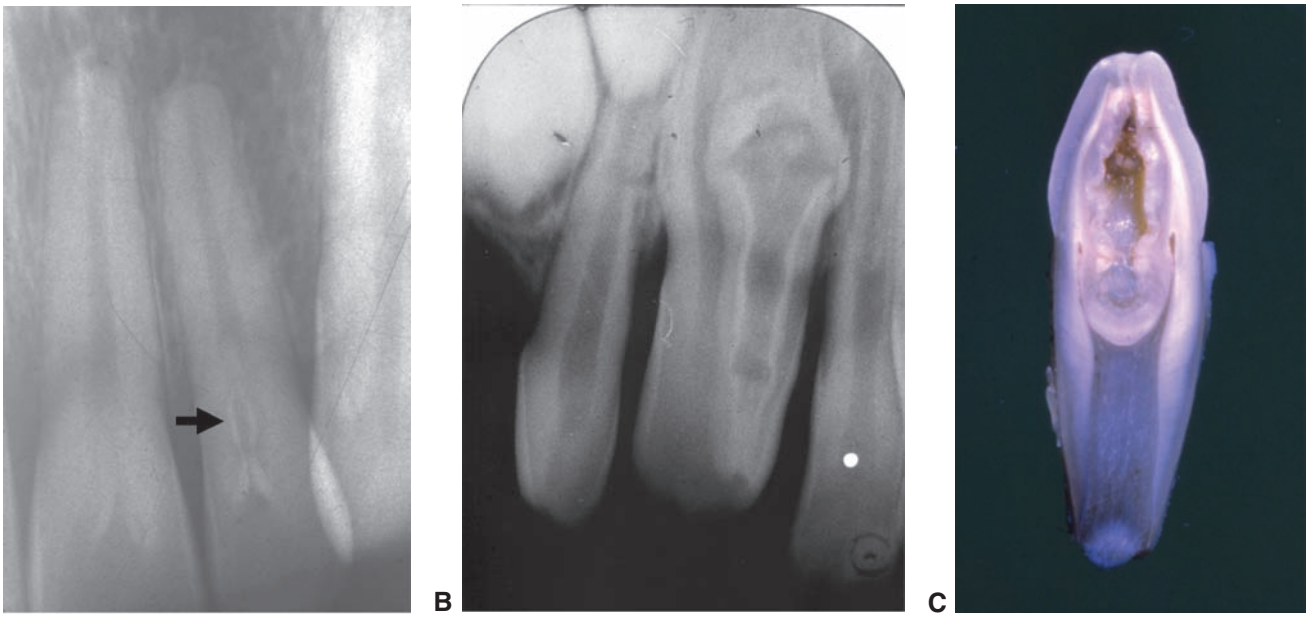


FIGURE 21.32. Dens invaginatus. **A**. A minimally affected lateral incisor tooth. The *arrow* highlights a small area of enamel invaginating from a pit in the cingulum area. **B**. A severely affected incisor results in marked deformation of the tooth shape. **C**. A cross section through the tooth shows the invaginating enamel within the crown of the tooth.

alveolar bone. In minimally affected teeth, the radiographic findings may be decidedly subtle, but in the most severe cases, a characteristic radiographic appearance is present. An area of increased opacity with the same density as the external enamel surface is visible in the central area of the crown and may extend down into the root structure.

Coronal dens invaginatus is clinically significant because in some instances the area of enamel invagination is deep enough to communicate directly with the dental pulp. This causes an opening to arise from the surface of the tooth into the vital portion of the tooth, allowing unimpeded access to the pulp by the microorganisms of the oral cavity. Pulpal necrosis with spread to involve the periapical region ensues, and patients may exhibit large periapical radiolucent lesions without an obvious cause. When the enamel invagination extends very deeply into the root area and perforates the root surface, the pulp chamber and root canal typically are separate from the defect, and the tooth may respond normally to vitality tests. In this situation, the normal pulpal architecture can be seen in a radiograph, with a layer of dentin separating it from the clearly visible, malformed area of the root.

Treatment of coronal dens invaginatus depends entirely on the depth of penetration of the enamel defect, whether or not it communicates with the dental pulp, and whether or not perforation of the root surface is present. If the invaginating defect is shallow and does not penetrate the pulp or perforate the root, simple restoration of the defect is advocated to prevent carious involvement. If the defect is deep enough to involve the dental pulp, endodontic therapy is warranted and may allow retention of the tooth. When root perforation is present, the situation is often very difficult to handle, and attempting conventional root canal therapy on the enamel tract may or may not alleviate the problem. Surgical endodontic therapy often ensues, and ultimately extraction of the tooth may be necessary.

Radicular dens invaginatus is quite rare. While the cause is not known with certainty, it likely represents an invagination arising from proliferation of Hertwig epithelial root sheath. The defect typically originates on the lateral surface of the root. The enamel formed within the invaginating defect arises from ameloblastic differentiation of the root sheath that is analogous to the formation of an enamel pearl. Radiographically, the defect may be difficult to visualize. Radicular dens invaginatus should be suspected though when there is an enlargement of the root without obvious cause. Treatment depends on the location of the defect along the root. If the defect is near the cementoenamel junction, it can become exposed to the oral environment, with resultant severe periodontal problems. In such instances, restoration is possible. When the defect occurs deeper on the root surface, no treatment is usually necessary.

Dentinogenesis Imperfecta (Hereditary Opalescent Dentin)

Dentinogenesis imperfecta is a hereditary disease that, as the name suggests, results in defective dentin formation. The dentin that is formed in patients with this disease has significantly fewer dentinal tubules than normal dentin. The tubules that are present are larger in diameter. In addition, the dentinoenamel junction is less convoluted, which reduces the mechanical retention of the enamel to the underlying dentin. For this reason, loss of enamel structure, which may mimic amelogenesis imperfecta, is a common additional finding in dentinogenesis imperfecta.

Dentinogenesis imperfecta shows an autosomal dominant hereditary pattern. Whites are disproportionately affected. The deciduous dentition is usually most severely affected, but the permanent teeth are invariably involved as well. In the permanent dentition, the later in life the teeth begin development, the less severe are the effects. Second and third molar teeth thus may show little evidence of the disease in some patients.

The characteristics of the teeth in individuals with dentinogenesis imperfecta are distinguishing. The teeth appear discolored, usually in shades of brown to gray, and they have a distinctive, almost silvery sheen in the early stages of the disease (Fig. 21.33A).

As enamel is lost from the surface, the dentin becomes more clearly visualized and the teeth have a yellow color. A thin, white-to-gray "outline," representing areas of retained enamel, is often present around the exposed yellow dentin. Since dentin is softer and less resistant to wear than enamel, once it becomes exposed, the teeth may show pronounced attrition, with loss of vertical dimension of occlusion. The radiographic appearance is also quite distinctive. The crowns appear bulbous because of a constriction at the cementoenamel junction area (Fig. 21.33B). Enamel may or may not be visualized covering the crown on the radiographs, depending on the degree of loss of the enamel already experienced. Quite characteristically, the pulp chambers and root canals are absent or greatly reduced in size. This is believed to result from excessive production of secondary dentin that obliterates the pulp tissue.

FIGURE 21.33. Dentinogenesis imperfecta. **A**. Clinical appearance of the teeth with *markedly brown*, opalescent appearance. The maxillary central incisors had previously been restored for aesthetic reasons. **B**. FA bitewing radiograph reveals the bulbous nature of the crowns, with constriction at the cervical neck of the tooth and obliteration of the pulp chambers and root canals.

The secondary dentin formation is stimulated by direct exposure of dentinal surfaces to the oral environment as a result of early enamel loss. The sclerotic changes in the pulp tissue may result in pulpal necrosis, eventuating in a periapical radiolucency without an obvious cause.

Treatment of patients with dentinogenesis imperfecta can be problematic. The loss of enamel may necessitate restoration of the teeth, but intracoronal restorations are often poorly retained. Crown coverage of involved teeth has also been advocated but predisposes the restored teeth to root fracture. If periapical inflammatory lesions occur, conventional root canal procedures may not be an option because of the obliteration of the pulp chambers and root canals, and surgical endodontic therapy may become necessary instead.

The dental changes associated with dentinogenesis imperfecta may be the only abnormality seen in a patient, but a large number of patients with these changes will prove to have an associated systemic disease of bone known as osteogenesis imperfecta. While the dental changes seen in these two disease processes are essentially identical, genetic analysis indicates that they are entirely separate diseases.

Dentinal Dysplasia (Rootless Teeth)

The name "dentin dysplasia" actually is applied to two disorders of tooth development, both of which result in alterations in the structure of dentin. These two forms are sublabeled (1) radicular dentin dysplasia (dentin dysplasia, type I) and (2) coronal dentin dysplasia (dentin dysplasia, type II). Neither of these two types is normally associated with dentinogenesis imperfecta or osteogenesis imperfecta. Certain other systemic diseases have been associated with tooth abnormalities that can closely mimic dentinal dysplasia. These diseases all seem to have one thing in common—a disruption in calcium control.

Radicular dentin dysplasia is a relatively infrequent disorder that shows an autosomal dominant pattern of transmission. It affects only the formation of the root by inducing disorganization in the deposition of the root dentin. When present in its most severe form, it produces an immediately recognizable radiographic picture consisting of a normally developed crown with minimal or no root formation. For this reason, the disorder is sometimes referred to as "rootless teeth." A range of affectation may be seen, however, and the classic radiographic features are not present in all instances. In many cases, the disorder may be recognized by roots that appear somewhat shorter and more tapered than normally expected combined with an abnormality in the

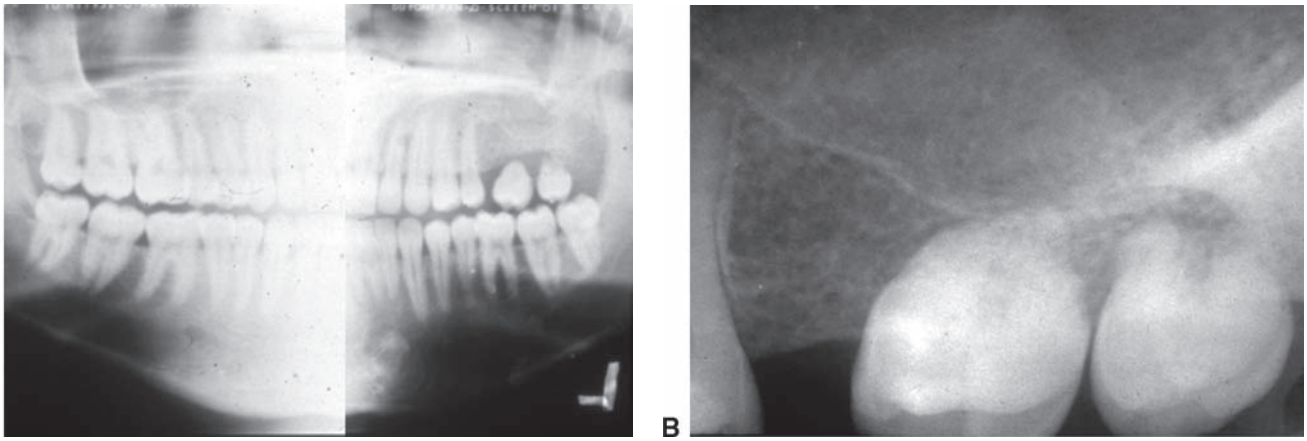


FIGURE 21.34. Dentin dysplasia. **A.** A local area of involvement in the left maxilla is present. The first molar had been lost several years previously due to excessive mobility. **B.** A periapical radiograph of the same patient as in **A** shows the almost complete lack of root development associated with the involved molar teeth.

shape of the pulp chamber and an absence of root canals. In its mildest form, the root length is within normal range, and the only indication of the disease may be the existence of a large pulp stone in the pulp chamber. Variation in the time of onset of the disease most likely accounts for the range in severity of root affectation. If the onset of the disease occurs very early in the cycle of root development, the roots will be severely shortened. If it occurs very late, the root will approach normal size (Fig. 21.34).

As with dentinogenesis imperfecta, the deciduous dentition is more severely affected than the permanent teeth. In the permanent dentition, considerable variability in the degree of involvement of the teeth may be seen within the same individual. One or only a few teeth may show evidence of the disease, with the remainder appearing normal radiographically. However, the entire dentition may be uniformly affected. Clinically, the teeth appear normal when visualized intraorally. Early and otherwise unexplainable mobility is a common presenting symptom, and the diagnosis is subsequently established when radiographs of the loose teeth are made. Premature loss of teeth, both deciduous and permanent, is also commonly cited as a presenting symptom in the most severe forms of radicular dentin dysplasia. The pulp chamber assumes a characteristic form in those teeth that have a shortened but sustainable root length, and it is described as a crescent-shaped lucency in the area of the cementoenamel junction. The root apical to the crescent-shaped lucency appears uniformly calcified without evidence of a root canal space. Due to the disorganization of dentin deposition with obliteration of the root canals, pulpal necrosis may occur with development of a periapical radiolucent lesion with no apparent cause. In affected teeth that have a nearly normal root length, the disorder is difficult to recognize and may go undiagnosed. The pulp chamber may appear normal in size. Notably, a large pulp stone is present in the pulp chamber, usually at the point where it funnels into the root canal area. The root appears bulbous in this region, but the enlargement is isolated to the area that surrounds the stone.

Treatment of radicular dentin dysplasia may be problematic, as there is little satisfactory recourse when root length is severely compromised. Extraction may be necessary if spontaneous loss of the involved teeth does not occur. Because of the extreme disorganization of the dentin and the lack of a negotiable root canal system, conventional endodontic therapy is often not a viable option. Creation of a canal space using rotary instruments with subsequent conventional endodontic filling has been attempted with some success. If the root length is sufficient and it is expected that the tooth can be retained, surgical endodontic therapy may also be an option, particularly in the presence of periapical pathosis.

Coronal dentin dysplasia shows many features in concert with dentinogenesis imperfecta, except that it appears to affect only the deciduous teeth significantly. Minimal changes are noted in the permanent dentition. The disease follows an autosomal dominant pattern of inheritance. The deciduous teeth have a brown-to-gray discoloration of the crown, with an opalescent sheen similar to that seen in dentinogenesis imperfecta. There is a constriction of the tooth at the cementoenamel junction area that makes the crown appear bulbous on radiographs. The pulp chambers and root canals are obliterated prematurely, but root length is not altered as it is in radicular dentin dysplasia. However, the roots may appear thinner than expected. Therefore, an original misinterpretation of the abnormality as dentinogenesis imperfecta is not unexpected. With eruption of the permanent teeth, that diagnosis becomes suspect. The permanent teeth are normal in color, do not show cervical constriction, and the pulp chamber and root canal spaces can be visualized on the radiographs. In fact, in contrast to dentinogenesis imperfecta, the pulp chamber typically appears enlarged and mimics the pattern seen in taurodontism. The pulp chamber extends apically into the superior portion of the root, creating a radiolucent area that is larger than expected for the involved tooth. The lucent pulp chamber is often described as rectangular to flame-shaped. Pulp stones may be seen within the enlarged pulp chamber.

Treatment of coronal dentin dysplasia is generally less problematic than that involved with radicular dentin dysplasia. The same problems encountered for dentinogenesis imperfecta are seen in trying to maintain the deciduous dentition, but once the permanent teeth erupt, treatment becomes easier. There is still an increased incidence of periapical inflammatory lesions associated with coronal dentin dysplasia. Since the pulp chambers are not obliterated, conventional endodontic therapy can be performed as needed on the permanent teeth. Pulp stones, if present, may increase the difficulty of conventional endodontic procedures to some degree.

Regional Odontodysplasia ("Ghost Teeth")

Regional odontodysplasia is a developmental abnormality that affects all of the calcified structures of the involved teeth. It does not show a recognizable hereditary pattern of transmission but instead is believed to be caused by a locally decreased blood supply to the developing tooth buds. This theory accounts for the typical clinical presentation in which several neighboring teeth in a limited region of the jaws are affected. In nearly all instances, the teeth involved are found to receive their blood supply from the same alveolar artery branch. Teeth that receive their blood supply from a different arterial branch but are immediately adjacent to the involved teeth appear entirely normal and unaffected. Without adequate blood supply, the inorganic elements necessary for calcification of the enamel and dentin matrices cannot reach the developing tooth, and the result is a poorly mineralized and incompletely formed tooth. Both clinically and radiographically, the teeth appear deformed. On clinical examination, the teeth show an irregular surface with discoloration in shades of gray to brown and may be mistaken for several of the other developmental abnormalities that alter the structure of the teeth. However, the radiographic appearance in regional odontodysplasia is diagnostic and easily recognized. The outline of the crown is irregular, and the pulp chamber appears markedly enlarged. A thin, malformed layer of poorly mineralized dentin is usually present, but it may be difficult to discern on the radiograph. The enamel is equally thin and irregular in outline. The roots are short and poorly formed; the apex is wide open. Thus, the overall appearance on radiographic examination is that of a mere phantom of a normal tooth, and the condition is often referred to as "ghost teeth" (Fig. 21.35).

Statistically, the most common area involved with regional odontodysplasia is the anterior maxilla, with the central incisor, lateral incisor, and canine teeth unilaterally being affected. All of these teeth are supplied by the anterior superior alveolar artery, a branch of the internal maxillary artery. Teeth affected with regional odontodysplasia, because of poor root development, often do not erupt. If the deciduous dentition is seen to be affected, their permanent successors are often involved. Most cases are diagnosed in the preteenage years. Involvement occurs more commonly in maxillary teeth than in mandibular teeth. On rare occasions, an apparently normal tooth will be seen between adjacent teeth affected by regional odontodysplasia. Cases of involvement of both the maxillary and mandibular teeth on the same side have been reported as well as bilateral involvement in the same jaw.

Treatment of teeth affected with regional odontodysplasia is difficult, and ultimately, extraction becomes necessary in a large number of cases. The extreme thinness of the enamel and dentin precludes intracoronal restorations or crown preparation in most instances. Endodontic therapy likewise can be difficult if root formation is minimal and the root apex is unformed. Early extraction of the involved teeth should be avoided, however, since the presence of teeth is necessary for normal growth and development of the bone of the alveolar process. Therefore, heroic attempts may be made to retain the teeth affected by regional odontodysplasia for as long as possible. Once the patient completes growth, extraction of the teeth with prosthodontic replacement can be accomplished in the later teenage or early adult years.

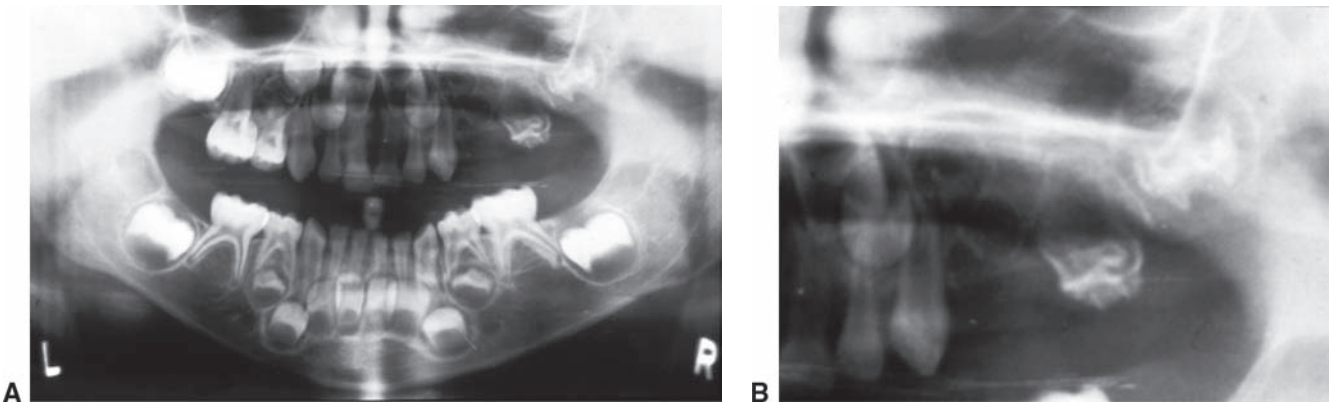


FIGURE 21.35. Regional odontodysplasia. **A.** The panoramic radiograph shows that the affected teeth are limited to the right posterior maxillary quadrant. **B.** A close-up view of the right maxilla reveals that the premolar and molar teeth are all affected. Note the irregular outlines of the crowns of the molar teeth.

Vitamin D–Resistant Rickets (Hypophosphatemia)

Vitamin D–resistant rickets is also known as hypophosphatemia. It is a hereditary disease that inhibits the body's ability to control and retain phosphates in the blood, resulting in a metabolic disturbance that affects all the calcified structures in the body. The disease is transmitted as an **X**-linked dominant trait; thus, there are an excess number of females affected because it is thought that most males who inherit the defective gene die in utero, at birth, or shortly thereafter. The clinical manifestations closely resemble those seen in classic rickets, a disease produced by inadequate dietary amounts of vitamin D. Unlike classic rickets, however, patients with vitamin D–resistant rickets do not show improvement with vitamin D therapy. Patients tend to be short in stature and commonly show bowing of the legs, due to an inability of the weakened bones to support the body's weight. Serum phosphate levels are also below normal.

As might be expected, vitamin D–resistant rickets also affects the structural relationships of the different parts of the tooth. On clinical observation, the teeth may show only subtle evidence of the disease. They appear normal in size, shape, and color. The time of eruption is often delayed. Patients will sometimes present with a dental abscess or other periapical pathology without an apparent cause for death of the pulp tissue. This symptom is directly related to the disease process. The deficiency in calcification involving the dentin results in abnormally extended pulp horns that often reach up to the dentinoenamel junction. Enamel defects, attrition, or shallow carious lesions allow exposure of the pulp horn, with unimpeded ingress of the oral microflora directly into the pulp chamber. Pulpal necrosis with development of a periapical radiolucency ensues. Radiographs may reveal the overelongated pulp horns and allow an accurate diagnosis to be made. The mandibular incisor teeth tend to show the radiographic changes most clearly, and the radiographic picture has been described as a "crow's foot" pulp because of the three-pronged appearance of the pulp horns in these teeth (Fig. 21.36).

Treatment of teeth affected by vitamin D–resistant rickets includes regular follow-up to monitor for periapical lesions. The hardness of the teeth is not affected, and the teeth are not prone to develop carious lesions. Restoration of carious lesions must be performed with great care, as exposure of the elongated pulp horns with routine intracoronal cavity preparation can easily occur. Prevention of carious lesions is therefore of particular concern, and sealants might be considered particularly beneficial for these patients. Endodontic treatment is performed when the teeth become pulpally involved.

Hypophosphatasia

Hypophosphatasia is a hereditary disease that shows a variety of patterns of inheritance. Autosomal dominant and autosomal recessive forms have been identified, with numerous different mutations within the gene linked to production of symptoms of the disease. The autosomal recessive pattern of inheritance shows the most severe effects and manifests earliest in life. The genetic defect alters production of alkaline phosphatase, an enzyme that functions in bone metabolism as well as in numerous other tissues. The patients show defects in bone deposition and calcification. Regardless of the inheritance pattern, the younger the patient is at the onset of the initial symptoms, the more severe the disease tends to be in its overall manifestation. Afflicted individuals tend to be short of stature with bowing of the legs, producing a clinical picture similar to that seen in rickets. The skull fails to calcify completely. Other symptoms are linked to an excessive calcium level in the blood, with calcification in the kidneys being a common complaint.

FIGURE 21.36. Vitamin D–resistant rickets. Pulp horns in the anterior mandibular teeth extend to the incisal edge. *Arrows* point out the "crow's foot" pattern seen in the superior portion of the pulp chamber.

The dental changes associated with hypophosphatasia are related to the inability of the cells of the periodontal ligament to produce cellular cementum. In the absence of cellular cementum, the periodontal attachment fibers cannot attach to the root surface, resulting in premature loss of teeth. The deciduous dentition in particular is affected. The inability to properly calcify the other layers of the tooth results in teeth with thin enamel and dentin and large pulp chambers. Radiographically, these teeth may appear as a shell of their normal form.

Dental treatment of patients with hypophosphatasia can be a challenge. The absence of cellular cementum makes retention of the teeth in the alveolus difficult, and the only option for treatment often is replacement of lost teeth with removable appliances. Because of the defect in bone formation, the alveolar ridges may show incomplete development, further hampering prosthodontic rehabilitation.

Alterations in the Color of Teeth

The color of the teeth may be altered by adherence of pigmented materials to the external surface. In this situation,

scaling of the teeth will allow relatively simple removal of the pigment, and the underlying normal tooth color will be restored, allowing easy recognition that the condition is caused by an external concretion. The products of cigarette, cigar, or pipe smoking are the most common external pigments encountered. As discussed above, alterations in the structure of the enamel and dentin may also produce color changes in the teeth. Lastly, incorporation of pigments into the calcified portions of the tooth or spillage of blood into the dentinal tubules may result in a color change. In these situations, cleaning, scaling, or polishing of the teeth will not remove the pigmentation, identifying it as a permanent intrinsic stain.

Fluorosis

Fluorosis was one of the earliest recognized conditions to produce an unsightly color change in the teeth. It was first perceived as a significant finding in communities in Colorado and was originally referred to as "Colorado brown stain" because of the typical color exhibited by the affected teeth. Detailed study of several populations affected revealed that the condition was caused by an excess quantity of fluoride in the drinking water. The extent of involvement was found to depend entirely on the total concentration of fluoride in the water, with severe effects routinely found when the fluoride levels exceeded five parts of fluoride per million parts of water. Lesser quantities of fluoride produced less discoloration, with levels of one part per million usually showing no deleterious effects on the color of the teeth. At lower fluoride concentrations, the color alteration is often found to be patchy. Enamel hypoplasia will accompany the brown discoloration at very high fluoride levels, with visible pitting of the enamel surface. A chalky surface with loss of translucence due to enamel hypoplasia is present at lower concentrations of fluoride (Fig. 21.37). Many other areas in the United States have also been found to have natural fluoride levels exceeding one part per million; therefore, the problem is not limited to Colorado.

FIGURE 21.37. Fluorosis. The teeth are diffusely involved. Note areas of *chalky white* enamel that lack the typical luster of enamel alternating with areas of *yellow-brown* discoloration. The patient grew up in West Texas in an area of high natural fluoride concentration in the water.

Interestingly, the teeth affected with fluorosis were found to have fewer caries than teeth without fluorosis. Even in the presence of enamel hypoplasia associated with very high levels of fluoride, an increase in carious lesions did not accompany the problem. Eventually, fluoride was proven to protect against the development of caries when present in sufficient concentration. Today, many toothpastes contain fluoride as an anticaries additive. In addition, most communities in the United States supplement their drinking water supply with fluoride, maintaining a level of approximately one part per million, as a public health initiative to prevent tooth decay.

Since teeth affected by fluorosis show lower carious activity, these patients tend to have fewer treatment needs overall. The discoloration is a major aesthetic problem for many patients, however. In the past, vital bleaching of the anterior teeth was often attempted to try to lighten the brown discoloration and improve the appearance, with quite variable results depending on the degree of involvement. For the most severely involved, crowning of the anterior teeth was often the only solution. Today, porcelain veneers offer a distinct improvement in the options available to patients with fluorosis.

Tetracycline Staining

Tetracycline is an antibiotic medication developed in the mid-20th century. Tetracycline was useful because it seemed to penetrate into bone better than penicillin; therefore, it was used as the drug of choice by many practitioners for infections involving bone. After its usage became more widespread and it was being increasingly prescribed for children, it became known that the tetracycline was also incorporated into any teeth that were undergoing calcification at the time that the medication was administered. Tetracycline can cross the placental barrier, and administration to pregnant women may result in involvement of the deciduous teeth of the developing infant. The affected teeth show a distinctive yellow-to-brown discoloration (Fig. 21.38A). The degree of involvement of the teeth was found to depend on the age at which the medication was administered, the dosage given, and the length of time the medication was taken. High doses of tetracycline also produced enamel hypoplasia because the incorporation of tetracycline disrupted the normal hydroxyapatite crystal structure of the enamel. Because of the deleterious effects on the teeth, the use of tetracyclines is now discouraged in pregnant women and in children under 8 years of age.

The color of the affected teeth was also found to vary, depending on the type of tetracycline given. Oxytetracycline tends to produce a yellow discoloration, while chlortetracycline generates a gray-brown color. Minocycline, a newer synthetic preparation, produces a green to gray to black color (Fig. 21.38B and C) and has been reported to produce discoloration of the teeth even after they are fully formed.

When viewed under ultraviolet light, teeth that have tetracycline incorporated into their crystalline structure will fluoresce a yellow to yellow-green color. As stated above, with the recognition of the deleterious aesthetic effects

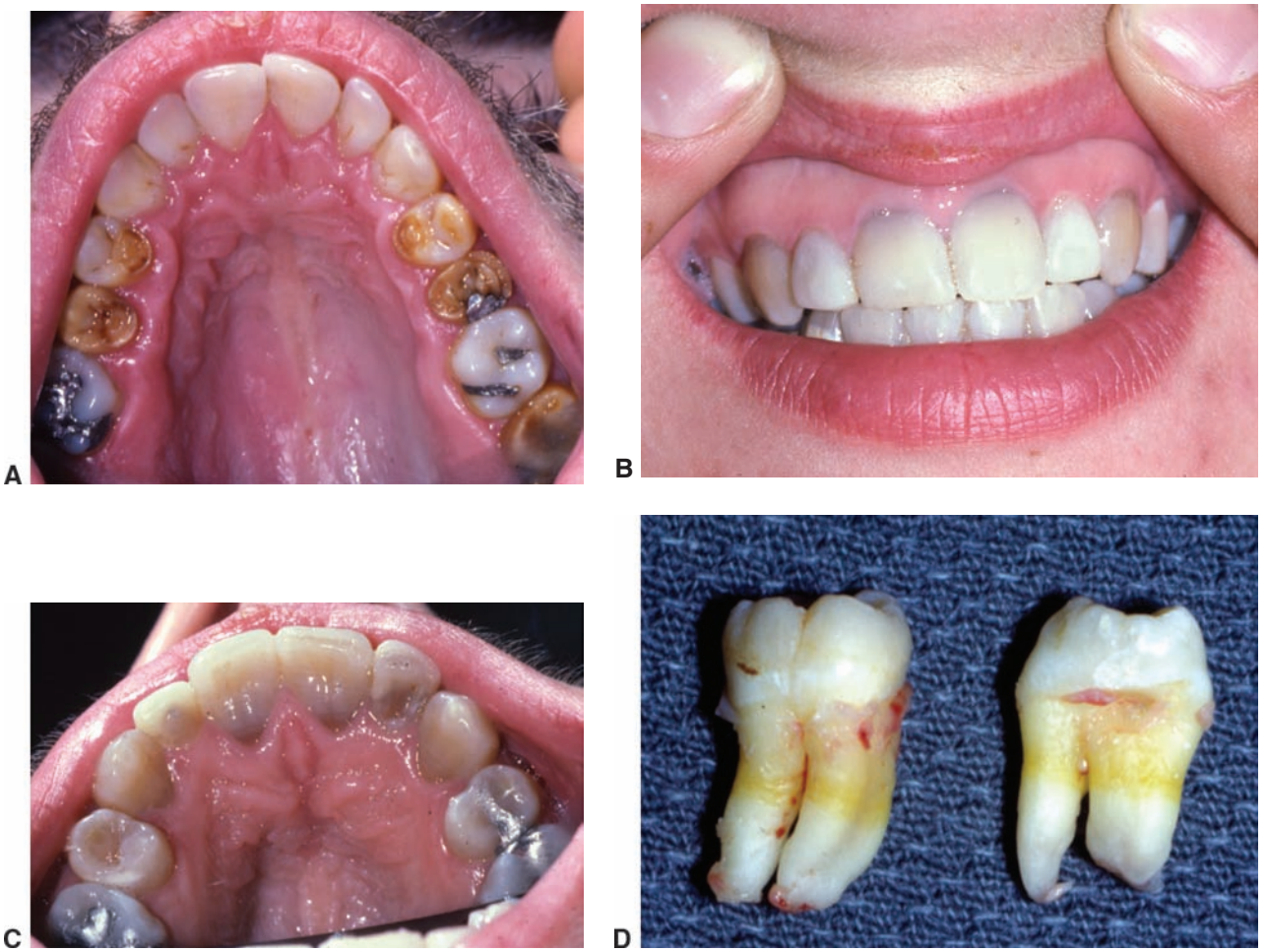


FIGURE 21.38. Tetracycline staining. **A**. Multiple teeth are affected bilaterally, showing hypoplasia and discoloration. The patient took tetracycline for a prolonged period around age 5. Note that the first molar teeth, which complete crown formation prior to that age, are not affected. **B**. There is discoloration at the cervical neck area of the central incisor teeth. The patient had a history of minocycline administration. **C**. Palatal view of the same patient as in **B** reveals more clearly the *dark brown* staining associated with minocycline. **D**. A *bright yellow* tetracycline ring is seen in the midroot area of these extracted third molar teeth. The patient took tetracycline for treatment of acne as a teenager.

of the use of tetracycline in children, its administration was significantly curtailed to the point that severe tetracycline staining of the teeth is not commonly seen today. Tetracycline is still used quite often in the teenage years to treat severe forms of acne. In many instances, the roots of the teenager's teeth are still forming when the tetracycline is administered. The fact that tetracycline was taken may be evident at the time of extraction of the wisdom teeth, when a bright yellow tetracycline ring is seen in the roots of the extracted third molars (Fig. 21.38D). However, if this acne treatment is instituted slightly too early and the roots in the area of the cementoenamel junction are still forming, the tetracycline discoloration may be seen as a dark area visible through the translucent free gingival margin at the neck of the tooth (Fig. 21.38C). This is particularly problematic with minocycline, which tends to produce a much darker discoloration of the tooth structure.

Hemolytic Anemia and Erythroblastosis Fetalis

Hemolytic anemia is defined as a systemic condition in which there is excessive and premature destruction (hemolysis) of red blood cells throughout the circulation. Hemolytic anemia can be produced by a variety of medical conditions, and a complete medical workup is often necessary to determine the specific cause. Conditions that are known to cause hemolytic anemia may be grouped into two categories: (1) systemic conditions that destroy red blood cells and (2) functional defects within the red blood cells themselves. Systemic conditions include overwhelming infections, toxins (cobra venom, brown recluse spider venom), enlargement of the spleen, chronic liver disease, hematologic malignancies such as leukemia and lymphoma, certain vitamin deficiencies (folic acid, vitamin B_{12}), some autoimmune diseases (specifically lupus erythematosus), and transfusion reactions. Functional defects of the red blood cells include hereditary diseases that affect the shape of the red blood cells (e.g., spherocytosis, ellipsocytosis), disorders of hemoglobin (e.g., sickle cell disease, thalassemia), and enzyme deficiencies (e.g., glucose-6-phosphatase deficiency).

Changes in the color of the teeth are produced by breakdown products of the destroyed red blood cells. Breakage of blood vessels within the dental pulp allows spillage of the hemolyzing red blood cells into the dentinal tubules. Degeneration of the spilled red blood cells results in

eventual degradation to hemosiderin, a brown pigment that in sufficient quantity can appear black. Since the degenerating red cells are within the dentinal tubules and cannot be phagocytized and removed, the brown-to-black discoloration is permanent and may be seen through the overlying translucent calcified layers. In addition, hemolytic anemia results in accumulation of bilirubin in the blood. Bilirubin is another breakdown product of red blood cell hemolysis. At elevated levels in the blood, it can be deposited in the calcified structure of teeth that are developing at the same time, producing a permanent blue-to-black discoloration. Adults tend to be most commonly affected by hemolytic anemia. Because the pulp chambers are often reduced in size in adults due to gradual deposition of secondary dentin, the discoloration associated with hemolytic anemia in this population is most often noted at the cervical areas of the teeth, which show a brown-to-black hue that may resemble the pattern seen in minocycline staining.

In the past, perhaps the most common manifestation of the hemolytic anemias was a condition termed erythroblastosis fetalis. The cause of this condition was found to be an incompatibility of the blood type of a developing fetus with the blood type of the mother. The mother's blood type was found to be Rh negative. The affected child was typically the second child born to the mother. The blood type of the firstborn child proved to be Rh positive, and the mother developed antibodies against Rh-positive blood at the time of delivery of the first child when the blood of the Rh-positive baby was mixed with her own. On becoming pregnant a second time, the blood of the second child, also Rh positive, is attacked by the previously developed antibodies in the mother's blood, which cross the placental barrier and produce widespread hemolysis in the baby. The breakdown of red cells causes an excess of circulating bilirubin in the blood, with deposition into the calcified tooth structures of the developing teeth. This produces pigmentation of the teeth that is analogous to the process in the other hemolytic anemias. In erythroblastosis fetalis, however, only the deciduous dentition is involved, and the pigmentation is severe, with all the crowns of the teeth being diffusely discolored. The discoloration may vary from green to blue to brown to black. An additional finding in erythroblastosis fetalis is a hypoplastic line in the enamel surface in the area of the teeth developing at the time of hemolysis. This is typically present on the deciduous canine or molar teeth and has been called the "Rh hump." Presently, erythroblastosis fetalis is rarely seen. Prenatal testing of the fetal blood type in Rh-negative mothers reveals the incompatibility in blood types in the first pregnancy and antiantigen gamma globulin is administered to the mother at delivery. The gamma globulin suppresses the development of Rh-positive antibodies in the mother's blood, preventing a future hemolytic crisis in subsequent pregnancies.

Treatment of teeth affected by hemolytic anemia is usually unnecessary unless there is significant visible discoloration that causes aesthetic concerns. In that case, treatment typically involves restorative procedures directed at masking the areas of discoloration.

Porphyria (Congenital Erythropoietic Porphyria)

Congenital erythropoietic porphyria is a rare genetically transmitted disease. It is inherited as an autosomal recessive trait, with the defective gene producing a disorder in porphyrin metabolism. Porphyrins are an integral component of hemoglobin and are found in large quantity in the red blood cells. The genetic defect causes increased synthesis and excretion of porphyrins. Uroporphyrins, a by-product of porphyrin metabolism, accumulate in the skin, blood, urine, and other body tissues (Fig. 21.39). Deposition occurs in the bone and teeth as well. Patients present with significant photosensitivity because the sun's rays react with the uroporphyrins that have been deposited in the skin. This results in the development of vesiculobullous lesions of the skin, even with only minimal sun exposure. The large blister-like lesions rupture and then heal with increased pigmentation, scarring, and mutilation. A compensatory response of the body is hirsutism and hypertrichosis—an increased proliferation and growth of hair in an attempt to protect the skin surfaces from further exposure to the damaging rays of the sun.

Oral findings in congenital erythropoietic porphyria include a reddish brown to gray to black discoloration of the teeth, depending on the quantity of uroporphyrins deposited in them. When these teeth are exposed to ultraviolet light, such as at night when a full moon is present, they fluoresce bright red.

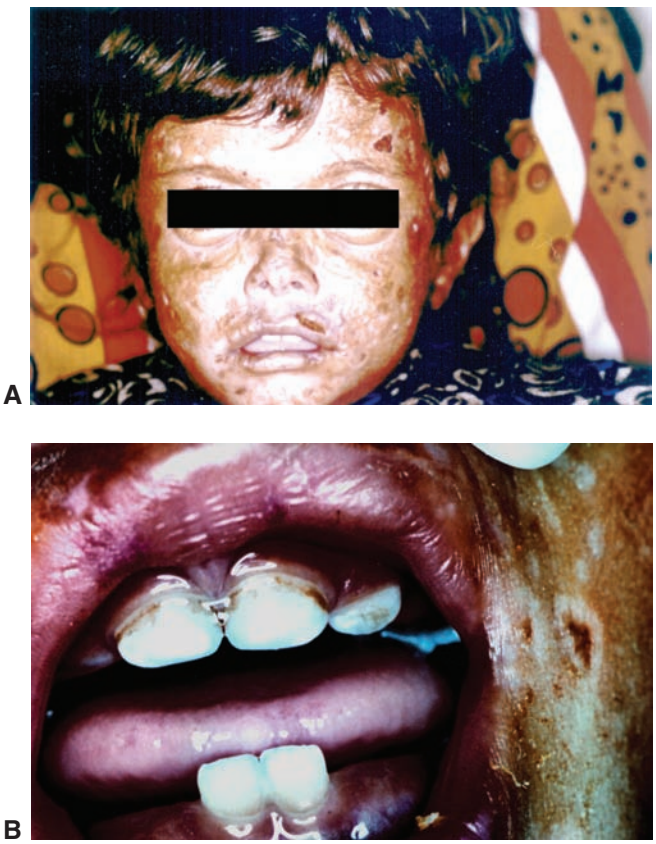


FIGURE 21.39. Porphyria. **A**. A young child with vesicles and scarring related to porphyria. **B**. Porphyria of the same child with red staining on the teeth from the effects of porphyria. Also note the vesicles and scarring on the facial tissue around the lips. (Photos courtesy of Dr. Faiez Hattab.)

As an autosomal recessive trait, congenital erythropoietic porphyria tends to occur in population groups with limited diversity, in which the recessive gene is present in more individuals than in the general population. During the 19th century, in several isolated areas of Europe, such population groups were known to exist. The constellation of findings associated with congenital erythropoietic porphyria may be responsible, therefore, for the mythology of the werewolf that originated from these locales.

SUMMARY

- This chapter details the various pathologic processes that affect the hard structures of the teeth.
- Pathology involving the teeth can be subdivided into those conditions that occur following normal growth and development of the teeth (postdevelopmental abnormalities) and those processes that occur during the period of tooth formation (developmental abnormalities). The developmental conditions are by far the most numerous.
- Postdevelopmental pathology typically produces obvious changes in the appearance of the tooth, either clinically or on radiographic examination, and normally manifests as a loss of tooth structure.
- While pathologic changes in the teeth of developmental etiology also normally produce some change in the appearance of the tooth, in a number of the developmental abnormalities the teeth may appear entirely normal on clinical evaluation.
- Developmental defects in the teeth can affect the number of teeth, the size of teeth, the shape of the teeth, the structural makeup of the teeth, or the color of the teeth.

CHAPTER REVIEW

Case Study 21.1

The patient presented in Figure 21.40 is a 43-year-old female who is in your practice today for dental exam and prophylaxis. You notice that she has a tooth that appears to be joined at the crown. The teeth are #25 and #26. Based on what is seen in the radiograph (Fig. 21.40B), what would you call this anomoly? What does the clinical image (Fig. 21.40A) along with the radiograph tell you about these teeth?

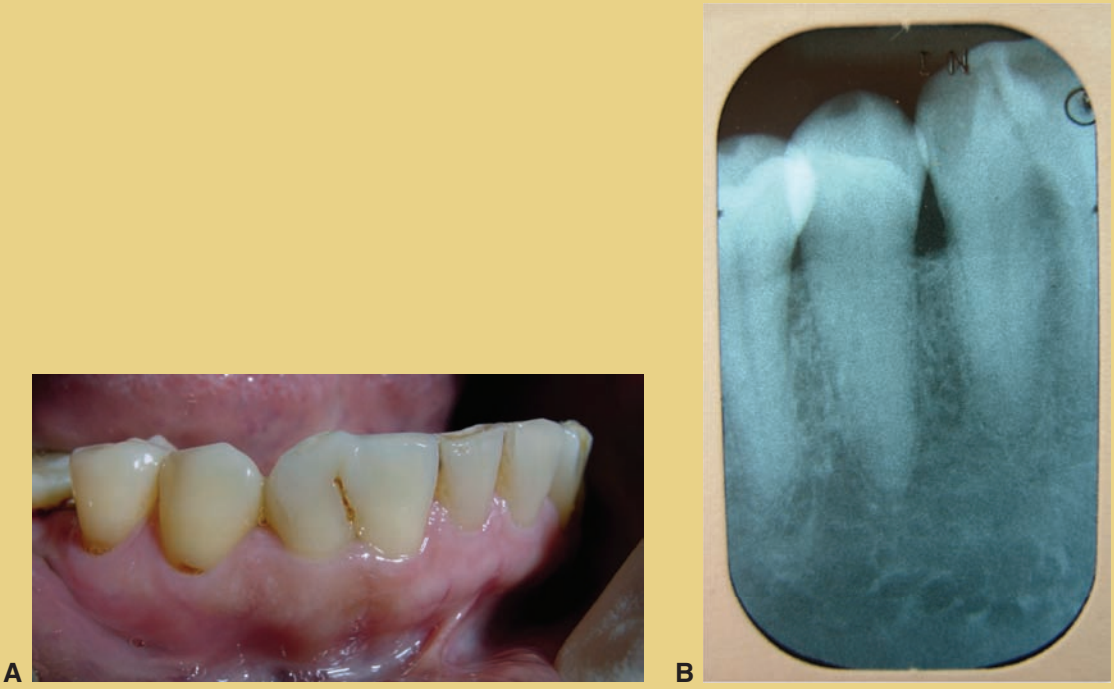


FIGURE 21.40. (Photo and radiograph courtesy of Dr. Gwen Cohen Brown.)

For answers and additional review activities, log in to **thePoint.lww.com**

Case Study 21.2

Please evaluate Figure 21.41 then respond to the questions that follow.

1. What do you notice about the maxillary lateral (tooth #7)?
2. Do you think that the image depicts an infection or a developmental defect, or is it a sign of a serious disease state?
3. Does the darker area connect with the pulp? Would you expect this tooth to test vital?
4. Would the fact that this happens to be a maxillary lateral incisor help you in making a decision regarding the etiology of this case?
5. What have you learned from this chapter that may assist you in narrowing your differential diagnosis?

For answers and additional review activities, log in to **thePoint.lww.com**

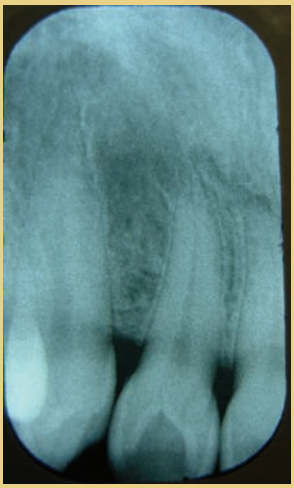


FIGURE 21.41. (Courtesy of Dr. Gwen Cohen Brown.)

Portfolio Possibilities

- Construct a patient education sheet for the parents of children who reside in an area where fluoride is not routinely added to the water supply, and for whom the dentist may want to prescribe fluoride supplements to decrease caries incidence. Include facts about the potential for tooth discoloration with excess fluoride and the need to strictly follow the dentist's or hygienist's instructions regarding dosage and frequency of administration.
- Develop an educational fact sheet that details the aesthetic restorative options available for patients with discoloration of the teeth (e.g., whitening kits, in-office bleaching, veneers, crown placement). List the advantages and disadvantages for each restorative method suggested.
- Construct a fact sheet for parents of adolescent children that emphasizes the typical dental changes seen in erosion caused by repeated vomiting associated with eating disorders. Include names and addresses of local resources and facilities that are available to assist in treatment of children with anorexia nervosa and bulimia.
- Create a visual aid (chart, drawing, or diagram) that can be given to parents of young children to illustrate the position of the developing permanent teeth in relation to the overlying deciduous teeth. Using the visual aid, devise a script that explains why early treatment of dental disease in deciduous teeth is important to prevent inflammatory induced enamel hypoplasia in the permanent dentition.

Media Menu

Web Sites

Basal Cell Carcinoma Nevus Syndrome Life Support Network
http://www.gorlinsyndrome.org/

Ectodermal Dysplasia Support Group
http://www.mdjunction.com/ectodermal-dysplasia

National Craniofacial Association: Cleidocranial dysplasia
http://www.faces-cranio.org/Disord/CCD.htm

Office of Rare Diseases Research: Langerhans cell histiocytosis
http://rarediseases.info.nih.gov/GARD/Condition/6858/Langerhans_cell_histiocytosis.aspx

Porphyria Support Groups and Information
http://www.familyvillage.wisc.edu/lib_porp.htm

Study Tools

Take advantage of additional online resources to help you study and ace your exams!

- Answers to case studies in the book
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- Expanded Media Menu with direct links to related Web sites and multimedia resources
- Supplemental references

thePoint Online resources and links are available at http://thepoint.lww.com/DeLong2e

Chapter 21 **LESION/CONDITION SUMMARY TABLE**

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Attrition	Wearing away of the tooth structure by tooth-to-tooth contact	Normal aging; can be influenced by diet; geographic location such as sandy regions. Hardness of enamel plays a role in severity.	Occlusal surfaces most often affected along with the incisal edges of teeth	NA	Occlusal adjustment may assist in some cases. Attention to diet and some modifications such as acid reduction, etc.	Maintenance appointments to monitor changes. Intraoral photographs for long-term comparison.
Abfraction	Considered a subcategory of attrition by some authors	Produced by the transmission of forces during mastication. Stress along the dentinoenamel junction causes flexing of thin enamel, which separates from the dentin and is lost.	Web-shaped defect, along the cervical areas of teeth Hypothesized to occur more often when occlusal forces are applied eccentrically such as lateral jaw movement and during bruxism	NA	Occlusal adjustment may assist in some cases. Treatment for bruxism may include night guards and is often effective. Stress reduction may play a role as well.	Maintenance appointments to monitor changes. Intraoral photographs for long-term comparison.
Abrasion	Pathological wearing away of the tooth structure, either mechanical or frictional. Using harsh oral products, hard toothbrushes, etc. Patient habits are also involved.	Cementum is softer than enamel; exposed root surfaces at the gingival margin are most affected. Horizontal brushing produces a V-shaped groove at the gingival margin.	A V-shaped depression is usually seen in the tooth structure. Occupational examples: beauticians who opened bobby pins with teeth, carpenters holding nails, etc. Nonoccupational habits such as tobacco chewing may be involved. Patients are usually asymptomatic.	NA	Discourage habits with alternative behaviors. Address occupational vs. nonoccupational causes. Some damage may need addressing after the habit is rectified.	The tooth structure may be weakened in severe cases. The cause will dictate the prognosis and progression of tooth damage.
Erosion	Loss of the tooth structure through contact with chemical agents	Softening of the tooth structure promoting wear of teeth. The buffering capacity of saliva is correlated with the degree of damage and ability to remineralize damage. Saliva flow affects the amount and length of exposure to the chemical.	Chemical erosion usually causes a smooth and polished appearance. Erosion may predispose the person to abrasion as well since it will soften the tooth structure. Protrusion of amalgam restorations above the level of surrounding tooth surfaces because the tooth structure has been lost	NA	Identify the etiology of the erosion and limiting exposure. Gastroesophageal reflux: treatment by a physician is needed. Disordered eating practices: refer to proper health care professional (physician and psychologist). Focus on area of damage to determine cause, e.g.: repeated vomiting usually produces more damage on the lingual/palatal surfaces.	The chemical problem needs to be solved before extensive restorative work is begun. In some instances, mouth guards and dental products may assist to keep further damage from occurring. The treatment is very individualized.
Pulpitis	Inflammation of the pulp	Caries, external trauma, occlusal trauma, dental procedures, extreme temperature changes, attrition, abrasion, and erosion	Pulpitis may be divided into reversible pulpitis, irreversible pulpitis, and hyperplastic pulpitis (pulp polyp).	Only seen on radiograph when inflammatory process spreads through the root apex and into the radicular bone	Determining the specific type of pulpitis is important since progression of the diseased pulp will continue.	Root canal therapy, possible extraction, and crowning of the tooth may be needed depending upon the type of pulpitis and whether it is reversible.

Chapter 21 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Pulp stones	Unknown with certainty but may be a function of normal aging	Alteration of cells in pulpal tissue causing calcification of some cellular aspect leading to a pulp stone	Asymptomatic and usually only seen on a radiograph	Appear as oval areas of opacity in the pulp chamber	No treatment is needed, and the patient is asymptomatic.	Pulp stones may make endodontic treatment more difficult should the need ever arise.
Internal resorption	Injury causes an influx of inflammatory cells within the pulp tissue.	Inflammation within the pulp tissue produces the osteoclasts that destroy tooth from within.	Observed as radiolucent area on radiograph and clinically as "pink tooth of Mummery." Vascular pulp tissue shown through the enamel produces pink color.	Highly inflamed and vascular pulp tissue	Treatment may consist of endodontics and is most likely when progression to "pink tooth of Mummery" has occurred.	Early intervention of all carious lesions and a good maintenance program for the patient
External Resorption	Trauma may cause Periodontal ligament. Cells to be activated and differentiate into osteoclasts. These cells break down tooth tissue.	External resorption is caused by 2 sources: (1) inflammation and (2) pressure against the tooth structure (ex: 3rd molar pressing against 2nd molar).	Any area of the tooth may be affected. The lower one-half of the tooth is most often affected.	Radiograph: shortened roots or a ragged or moth-eaten border where it abuts against tooth structure. Tooth may show both radiopaque and radiolucent areas.	Large areas of damage will necessitate removal. Shortening of the roots does not require treatment unless there is extreme damage and mobility.	Careful maintenance and follow-up of all teeth are needed.
Enamel hypoplasia	Inflammation and developmental causes and trauma to the developing tooth have been cited as well.	Involves follicular tissues that surround the crown of tooth at time of production and calcification of the enamel matrix. The crown of developing tooth is engulfed in noxious environment produced by inflammation.	Almost always seen in premolar teeth but may affect any teeth with an infected deciduous precursor. Permanent molar teeth rarely affected. Enamel tooth bud of developing tooth is damaged. Anterior teeth rarely involved since formation of enamel occurs earlier and they are less likely to develop caries during early years.	Pitting, grooving, or shallow cavitations discoloration (called "Turner tooth"). Inflammation-induced enamel hypoplasia: single tooth. Developmental hypoplasia: multiple teeth.	Most concerns are those of aesthetics in relation to the tooth or teeth.	Careful maintenance and any restorative work should be completed when needed and maintained.
Anodontia	2 categories: (1) not associated with genetic or systemic disease; (2) genetic inherited conditions	Certain teeth are found to be missing more often: 3rd molars, maxillary lateral incisors, and mandibular 2nd premolars.	Radiographs are needed as well as a good health history. Extracted teeth are not considered anodontia.	Hereditary hypohidrotic ectodermal dysplasia is associated with decreased numbers of teeth. Other syndromes should be considered as well.	Maintenance and referral if needed	Careful maintenance and any restorative work should be completed when needed and dentition maintained as much as possible.
Hereditary hypohidrotic ectodermal dysplasia	Most common genetic disease causing missing teeth. X-linked recessive syndrome. Most patients are males.	If males inherit disease on X chromosome, features will be seen. Homozygous females are affected even more severely. Heterozygous females are carriers and show no evidence of the disease.	Skin, eyelashes, eyebrows, and hair will be fine and sparse. Large lips are present. Sweat glands are affected, and salivary tissue may be also.	Oligodontia (6 or more missing teeth) is characteristic and often a distinguishing figure.	Referral and close working relationship with physician treating the patient	Follow-up and maintenance for dental issues

continues

Chapter 21 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Bloch-Sulzberger disease (incontinentia pigmenti)	X linked dominant genetic disease. Manifests with skin abnormalities, neurologic conditions, and bone defects.	Most patients are females. Anodontia is significant.	Teeth affected in 60–80% of patients	Peg-shaped anterior teeth and delay in eruption patterns	Recognition of the syndrome and referral or treatment	Follow-up and maintenance
Hyperdontia	May be autosomal dominant and exhibits increased numbers of teeth	Hyperdontia may be subdivided into 2 categories: supernumerary and accessory.	Supernumerary teeth occur: 1st most commonly as mesiodens and 2nd most commonly as distomolars.	Accessory teeth usually are small and often have a conical crown.	Recognition is important and removal of the supernumerary tooth is usually needed. May block normal eruption	Follow-up and maintenance
Cleidocranial dysplasia (dysostosis)	Genetic disease—autosomal dominant	40% of cases have neither parent with disorder—it is thought to be a new mutation in some cases.	Small stature, skeleton affected, underdeveloped jaw, multiple supernumerary teeth Eruption is prevented, and crowding is extensive.	Cleft palate, multiple impacted teeth are often present. Radiographically distinctive in the number of supernumerary teeth	Treatment for dental issues. Some may need to be performed in a hospital setting.	Good dental treatment and follow-up
Gardner syndrome	A genetic disease inherited from a defective gene of a parent	Autosomal dominant disease	Multiple osteomas involving skull, face, and jaws. Cancerous intestinal polyps are preceded by radiographic evidence of osteomas. Multiple odontomas may also be seen.	Angle of mandible and ramus are often involved with dense radiopaque evidence of osteomas.	Early recognition is important since cancerous polyps are preceded by skull/jaw lesions with recognition of osteomas as a sign of the disorder. Polyps treated preventively to ensure that the growths do not progress.	Good dental care, follow-up, and monitoring
Microdontia	Generalized microdontia is very rare. Microdontia is usually localized.	The teeth affected by hypodontia are generally those affected by microdontia.	The third molars are most frequently affected followed by the maxillary lateral incisors. The laterals are termed “peg laterals” and usually present with bilateral symmetry.	NA	Crowns are often needed for the peg laterals for aesthetic concerns. Usually, there is no real issue with either of these types of microdontia.	Good dental care and maintenance
Macrodontia	May be localized or generalized. If generalized, occasionally associated with pituitary gland tumor	If associated with pituitary giantism, individuals may be exceedingly tall.	Increase in the size relative to what is considered normal	The teeth are large but may be in proportion to the size of the person.	Fusion of the teeth and supernumerary teeth are most often found as an anomaly. Gemination may occur.	Close clinical observation with radiographic evaluation
Shovel-shaped incisors	Occur more in East Asians, Siberian Eskimos, Alaskan Eskimos, and Native Americans	This entity has a genetic component since it is seen more often in certain ethnic groups.	The entity has a thickened mesial and distal marginal ridge that resembles a shovel when viewed from above the incisal edge.	Radiographic appearance is unremarkable.	Keep in mind that the shovel-shaped teeth are associated with dens evaginatus and dens invaginatus.	Continued monitoring and a good maintenance program
Cusp of Carabelli	Developmental accessory cusp	Male prevalence, highest in whites and rare in Asians	Found on maxillary 1st molar teeth as an elevation on the mesial lingual cusp	No radiographic significance	Grooves in cusp may make them more susceptible to caries.	Evaluate for any caries at maintenance appointments
Talon cusp	Developmental accessory cusp Resembles the claw of a bird of prey	Found on cingulum of maxillary incisor or canine teeth Elongated structure that may reach the incisal edge	May be bilateral or affecting single tooth	Additional cusp is seen on a radiograph.	The elongated cusp contains a pulpal extension, making adjustment of the height of accessory cusp difficult and risking pulp exposure; endodontic therapy may be necessary.	Good monitoring and maintenance

Chapter 21 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Doak's cusp	Developmental cusp that is sometimes found on the facial surface of molars	A pulp horn usually extends into the cusp.	The cusp is on the facial surface and a groove may be noticeable fusing to the tooth surface.	The cusp is usually not visualized on a radiograph.	Caries in and around the cusp may be present.	Good monitoring and maintenance
Dens evaginatus	Developmental cusp found in the central groove of a tooth	A pulp horn usually extends into the cusp. Often the cusp may affect occlusion.	Mandibular teeth most often affecte. Bilateral involvement is occasionally seen clinically.	It is difficult to identify the cusp on a radiograph.	Accessory cusp may interfere with occlusion. Care must be taken so that the pulp within the cusp is not damaged.	Monitoring and maintenance
Gemination	Developmental: crowns arise from a single root system.	A tooth bud attempts to split into 2 separate teeth. Clinically, there appears to be a supernumerary tooth.	Occurs on the maxillary anterior teeth and does not occur in the molar region	The radiographic appearance confirms the sharing of the root system.	No dental implications are suggested unless endodontic procedures are needed.	Monitoring and maintenance
Fusion	Two tooth buds fused together. Separate roots, but fused at the crown and appear to have a single crown	During dental matrix formation, tooth buds contact and are fused together. Joined by shared dentin	The crown appears larger than normal. Most common in the anterior region of the jaws. But, more common in the deciduous dentition	Radiographic evidence will support the fact that there will be 2 root systems.	No dental implications, but radiographs confirm diagnosis	Monitoring and maintenance
Congenital syphilis	Venereal disease causes offspring to have notched incisors and berry-shaped molars.	Passed from pregnant mother to fetus; caused by Treponema pallidum which alters the developing tooth germ.	Hutchinson incisors: notched incisal edge. Narrow width. "Mulberry molars" have a:" berry-shaped appearance on the occlusal surface of the 1st permanent molar.	The clinical aspect is usually diagnostic.	Identification is important: a child born in the second stage of syphilis may have additional disorders such as deafness, eyesight problems, etc.	Monitoring, referral for other health-related problems, and maintenance
Abnormalities affecting the roots of the teeth	Included are accessory roots, dilacerations, enamel pearl, taurodontism, concrescence, and hypercementosis	Caused by either abnormality in alterations of Hertwig root sheath or an overproduction of cementum	All the entities either cause a visible growth or distortion of the root of the tooth.	Radiographic examination will assist the clinician in the diagnosis.	Extraction and root canal will be more difficult in most cases. Also if endodontic procedures are needed, the endodontist may have more difficulty.	Patient information would be needed when called to the patient's attention. Monitoring and maintenance
Enamel hypoplasia	Malfunction of the ameloblasts that produce enamel during tooth development	Due to systemic illness, malnutrition, or environmental factors	Multiple cavitations and discoloration are evident.	Clinically apparent to the practitioner	The patient may be concerned about the appearance of the teeth and ask for treatment with restorative procedures.	Know tooth eruption and formation patterns to determine the cause of hypocalcification.
Amelogenesis imperfecta	Defective enamel on the teeth. Dentin and cementum are not affected.	Genetic basis. Each stage of enamel development is controlled by separate intricate genetic mechanisms. Numerous variations occur.	Most commonly, the main cause of amelogenesis imperfecta is a defect in deposition of enamel matrix.	Multiple teeth with significant discoloration and pitting; enamel seems to flake off of the tooth. Deciduous and permanent dentition affected. The density of the enamel becomes thinner.	The aesthetic concerns are usually paramount for the patient.	Sensitivity may be an issue; bleaching will not whiten teeth, since yellow dentin will begin to show through the thin enamel. Restorative procedures may be warranted.
Dens invaginatus (dens in dente)	The normal layering of the dentin and the enamel is disrupted.	Results in an abnormality in the enamel organ. The normal enamel layering on the outside of the tooth is disrupted and becomes invaginated within the tooth crown.	The maxillary lateral incisor is most commonly affected. May be found in about 10% of all patients	The invagination may result in an enamel pearl that has contact with the pulp. Pulp necrosis may occur. Radicular dens invaginatus is quite rare.	Aesthetics can be a concern. Treatment depends solely on the severity. Sometimes Root canal therapy or surgical procedure may be needed. In shallow defects, restorative material will seal the invagination off from bacteria and the normal flora of the mouth.	Periodic radiographs and monitoring

continues

Chapter 21 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Dentinogenesis imperfecta	Hereditary disease (autosomal dominant) resulting in defective dentin formation	Dentinal tubules are fewer in number, but larger in diameter. Usually in whites	Deciduous teeth are affected and permanent dentition as well. Pulpal necrosis is an issue. Surgical endodontic therapy may be needed.	Dentin is soft so attrition is common. Pulp chambers show obliteration. Patients may have osteogenesis imperfecta (systemic bone disease).	Aesthetics is an issue. Crowns often predispose the patient to root fractures. Restorative work is individualized.	Maintenance and monitoring
Dentinal dysplasia	Two forms: Type 1: radicular autosomal dominant pattern Type 2: coronal deciduous teeth more severely affected	Associated with other disease states, but the commonality is a disruption in calcium control in both types.	Type 1: affects the root deposition of dentin Roots are tapered, minimal, or even nonexistent. Absence of root canals or pulp canal Type 2: affects the crown of deciduous teeth Permanent teeth are least affected.	Clinically: mobility may be noted. Radiographs: shortened roots or no roots; oral view may appear normal. Premature loss of teeth may be found. Type 2: pulp chamber appears enlarged. Increased risk of periapical inflammatory lesions.	Extraction or endodontic root canal depending upon the severity. Type 2 may exhibit pulp stones making endodontic procedures difficult. There are fewer problems in the Type 2 coronal variation when the permanent teeth appear. Deciduous teeth are brown, gray with an opalescent sheen.	Continued maintenance and monitoring
Regional odontodysplasia (ghost teeth)	Developmental abnormality that affects the calcified structures of all involved teeth	It is believed to occur because of inadequate blood supply to the developing tooth bud.	Teeth appear to be deformed and only a faint shell of a normal tooth is detectable. On a radiograph, the pulp chambers appear larger than normal. The teeth have a malformed, thin layer of enamel and dentin.	Anterior maxilla is most often involved.	Retention of teeth is needed so that a normal growth pattern of all dentition occurs.	Individualized treatment and good maintenance program
Vitamin D–resistant rickets Hypophosphatemia	Hereditary disease Transmitted by an X-linked dominant trait	The patient is unable to retain and control phosphates in the blood.	Pulp horns appear to reach the incisal edge of the tooth.	"Crow's feet" patterns are seen in the superior portion of the pulp on a radiograph.	Periapical lesions may result with any damage to a pulp horn. Attrition or enamel defects may cause pulp damage.	Caries control is paramount since even shallow restorations may damage the pulp horns. Frequent recalls are needed to detect early caries.
Hypophosphatasia	Autosomal dominant and autosomal recessive forms	A genetic defect alters the production of alkaline phosphatase, an enzyme needed for bone metabolism and numerous other tissue functions.	The younger the patient, the more severe the disorder. Individuals are shorter, bowed legs as seen in rickets. Excessive calcium in the blood	Inability to produce cellular cementum results in premature loss of teeth, particularly deciduous teeth. Radiographically, teeth appear as a shell of a tooth.	Replacement of teeth with appliances is often needed. Alveolar ridges may not form correctly. This adds to the problem of maintaining appliances.	Treatment can be challenging. Absence of cellular cementum makes treatment difficult.

Chapter 21 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Fluorosis	Caused by excessive quantity of fluoride in the drinking water	When fluoride exceeds 5 parts of fluoride per million parts of water. Less than 1 part per million show no effects on the color.	A chalky surface with loss of translucence (enamel hypoplasia) is present in lower concentrations.	Teeth have fewer caries. 1 part per million is the normal concentration in drinking water.	Porcelain veneers are placed on the anterior teeth in severe cases. Bleaching has varying effects depending upon severity.	Caries will be reduced in patients with fluorosis.
Tetracycline staining	Tetracycline penetrates into the bone. It is incorporated into the teeth that are calcifying.	Tetracycline can cross the placenta. Enamel hypoplasia can also be found with the use of tetracycline. Pregnant women and children under 8 should not use this product.	The teeth present with a brown-to-gray color. With the use of some synthetic preparations, such as minocycline for acne, the medication produces what has been called "black bone staining." The product can be incorporated even after tooth development.	Teeth roots may be forming and retain the dark color that is seen through the gingiva when tetracycline or the synthetic forms are administered during the early years.	Depending upon the severity, the patient may be able to bleach or have porcelain veneers placed.	There are no other detrimental effects to the teeth. Maintenance is all that is necessary.
Hemolytic anemia and erythroblastosis fetalis	A systemic condition in which there is excessive or premature destruction of the red blood cells (RBC)	Conditions known to cause this fall into 2 categories: (1) systemic conditions that destroy RBC and (2) functional defects with the RBC themselves	Discoloration of the teeth may result because of the break down of the blood cell products. Black/brown discoloration In erythroblastosis fetalis, developing baby, the break down of the RBC and the circulating bilirubin in blood is deposited in the developing tooth structure. It crosses the placenta.	Adults tend to be affected most often. The cervical area of the teeth may appear brown. The teeth in erythroblastosis fetalis may be very dark.	Restorative procedures to address aesthetic concerns	Maintenance and monitoring No other dental concerns other than discolored teeth
Porphyria (congenital erythropoietic porphyria)	Rare genetically transmitted disease	Autosomal recessive trait Porphyrins are a component of hemoglobin found in large quantities in RBCs. There is an increased synthesis and excretion of porphyrins in patients with porphyria. The by-product of porphyrin is uroporphyrin and this accumulates in skin, urine, and body tissues—teeth.	Patients are photosensitive and have skin ulcerations, scaring, pigmentation, and hirsutism. The teeth have a red hue and the urine is bright red.	The teeth show a reddish color because uroporphyrins, a by-product of porphyrin metabolism, fluoresce.	The high-carbohydrate diet that is recommended to these patients makes them more prone to caries. Closely monitoring for caries. Suggest SPF lip balms and sunscreens. Contraindications are lidocaine, mepivacaine, barbiturates, mercury compounds, aluminum, copper, alcohol-containing rinses, and dapsone.	High maintenance to control for caries. Emotional support for a rare disease is always important.

CHAPTER 22

HIV and AIDS

KEY TERMS

Retrovirus
Seroconversion
Seropositive
Opportunistic
Viral load

LEARNING OUTCOMES

1. Describe the human immunodeficiency virus (HIV).
2. Describe HIV acute primary infection.
3. Define seroconversion and discuss what type of diagnostic tests for HIV can be done prior to and after seroconversion.
4. Describe the clinical latency period.
5. List systemic opportunistic infections/conditions associated with acquired immunodeficiency syndrome (AIDS).
6. Briefly describe highly active antiretroviral therapy (HAART).
7. List six oral lesions associated with HIV infection.
8. Describe the clinical features of pseudomembranous candidiasis.
9. List two other clinical conditions that should be included in a differential diagnosis of a patient with hairy leukoplakia.
10. Describe the clinical appearance of human papillomavirus lesions within the oral cavity.
11. List the two most common malignancies associated with HIV infection.
12. List the most common location for Kaposi sarcoma (KS) lesions within the oral cavity of an immunocompromised patient.
13. Compare and contrast the clinical appearance and common characteristics of minor versus major aphthous ulcers.
14. List current treatment modalities for the management of patients with recurrent herpetic stomatitis.
15. Describe the clinical features of linear gingival erythema.
16. Discuss the clinical presentation of patients with necrotizing ulcerative periodontitis (NUP).

CHAPTER OUTLINE

HIV Infection
- Human Immunodeficiency Virus
- Pathogenesis
- Therapy

Oral Manifestations of HIV
- Candidiasis
- Hairy Leukoplakia
- Human Papilloma Virus Lesions
- Malignancies or Neoplastic Lesions
- Oral Ulcerations
- Periodontal Diseases
- Salivary Gland Disease and Xerostomia

RELATED CLINICAL PROTOCOLS

#4 Treating Patients with Xerostomia
#5 Diagnosing and Treating Patients with *Candida*
#20 Oral Health Care Management for the Patient with HIV/AIDS
#26 Helping Relationships for Dental Hygienists
#27 Motivational Interviewing for Behavior Change

HIV Infection

In 2009, 33.3 million people across the globe were living with human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS). In the United States, over 1 million individuals are presently living with HIV/AIDS, an estimated 21% of whom are unaware of their condition. Those at highest risk in the United States are (1) men who have sex with men, (2) women, and (3) youths (NIAID, 2011).

Human Immunodeficiency Virus

The HIV is a **retrovirus**, meaning it contains a central core of RNA instead of DNA as its genetic material. Once the retrovirus infects a cell, it will use the enzyme reverse transcriptase to change its RNA into DNA. The viral DNA then integrates with the DNA of the host cell, forcing the cell to replicate the virus instead of performing its normal activities. HIV belongs to a subgroup of retroviruses called Lentivirus. Viruses in this group are considered "slow" viruses because there is a long period between initial infection and the appearance of clinical symptoms of disease.

Pathogenesis

Once the person is infected, the virus begins destroying the targeted cells, usually the CD4 T cells. There is an immediate severe drop in CD4 levels during this phase. Up to 70% of individuals infected with HIV experience clinical symptoms about 2 to 4 weeks after exposure known as the acute primary infection or sometimes the acute seroconversion syndrome. Most report flu-like symptoms of fever, fatigue, sore throat, and sometimes rash that spontaneously resolves after 2 to 3 weeks. During this time, the individual's immune system starts to produce antibodies to the HIV, and other immune system cells such as the killer T cells (CD8) fight against the infection. **Seroconversion** occurs at the point in time when the level of antibody against HIV is high enough to be detected in the individual's blood. Diagnostic tests based on antibody levels such as the Western blot and the enzyme-linked immunosorbent assay (ELISA) are effective after seroconversion. Tests that identify HIV genetic material in the blood can be used to identify recently infected individuals who have not yet seroconverted.

Eventually, the immune response is able to fight the virus, the CD4 T cell level rebounds, and the level of HIV detectable in the blood decreases. This is called clinical latency, and while symptoms may be undetected during this phase, the virus is actively being produced within the lymphoid organs and the person has the ability to transmit the virus. Persistent generalized lymphadenopathy (PGL) is one clinical finding that may be observed during the latency period of HIV. PGL often affects the lymph nodes of the head and neck area and might be the initial manifestation of HIV infection a dental professional could identify. The latency period varies with each individual and may last a very short time or may last for 12 or more years. Researchers have found one gene (CCR5) that seems to influence how HIV infection occurs or progresses in humans (NIAID, 2011). HIV disease progresses very slowly in individuals with a mutation in one of the two copies of this gene; if both copies of the gene are mutated, the individual seems to be immune to infection with HIV. This gene is the subject of much research at this time. Eventually, the virus devastates the immune system and a multitude of symptoms may manifest, collectively known as AIDS.

In AIDS, the **viral load** (level of viral RNA circulating in the blood) increases dramatically and the number of CD4 T cells drops just as dramatically, leaving the individual severely immunocompromised and at risk for many infections and other disorders that the immune system plays a role in preventing. The drop in CD4 T cells has far-reaching effects on the rest of the immune system by reducing the function of CD8 T cells, natural killer cells, and macrophages, as well as reducing the ability of B cells to produce antibody in response to new antigens. Most of the conditions associated with AIDS are considered to be "**opportunistic**," in other words, they take advantage of the compromised immune system. In immunocompetent individuals, these conditions occur either rarely or result in much less severe disease than those who are HIV positive. Laboratory criteria for defining HIV infection and AIDS are listed in Table 22.1. A diagnosis of AIDS can be made with either laboratory confirmation of HIV infection and a CD4+ T-lymphocyte count of less than 200 cells/μL and/or laboratory confirmation of HIV infection and the presence of at least one of the 26 AIDS-defining conditions listed in Box 22.1.

TABLE 22.1

Surveillance Case Definition for HIV Infection Among Adults and Adolescents (Aged ≥13 Years)—United States, 2008

Stage	Laboratory Evidence[a]	Clinical Evidence
Stage 1	Laboratory confirmation of HIV infection *and* CD4+ T lymphocyte count of ≥500 cells/μL *or* CD4+ T lymphocyte percentage of ≥29	None required (but no AIDS-defining condition)
Stage 2	Laboratory confirmation of HIV infection *and* CD4+ T lymphocyte count of 200–400 cells/μL *or* CD4+ T lymphocyte percentage of 14–28	None required (but no AIDS-defining condition)
Stage 3 (AIDS)	Laboratory confirmation of HIV infection *and* CD4+ T lymphocyte count of <200 cells/μL *or* CD4+ T lymphocyte percentage of <14[b]	*or* documentation of an AIDS-defining condition (with laboratory confirmation of HIV infection)[b]
Stage unknown[c]	Laboratory confirmation of HIV infection *and* No information on CD4+ T lymphocyte count or percentage	*and* no information on presence of AIDS-defining conditions

[a]The CD4+ T lymphocyte percentage is the percentage of total lymphocytes. If the CD4+ T lymphocyte count and percentage do not correspond to the same HIV infection stage, select the more severe stage.
[b]Documentation of an AIDS-defining condition supersedes a CD4+ T lymphocyte count of ≥200 cells/μL and a CD4+ T lymphocyte percentage of total lymphocytes of ≥14. Definitive diagnostic methods for these conditions are available in Appendix C of the 1993 revised HIV classification system and the expanded AIDS case definition (CDC. 1993 Revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. MMWR 1992:41[No. RR-17]) and from the National Notifiable Diseases surveillance system (available at *http://www.cdc.gov/epo/dphsi/casedef/case_definitions.htm*).
[c]Although cases with no information on CD4+ T lymphocyte count or percentage or on the presence of AIDS-defining conditions can be classified as stage unknown, every effort should be made to report CD4+ T lymphocyte counts or percentages and any identified AIDS-defining conditions can be reported as recommended. (Council of State and Territorial Epidemiologists. Laboratory reporting of clinical test results indicative of HIV infection: new standards for a new era of surveillance and prevention [Position Statement 04-ID-07]; 2004. Available at *http://www.cste.org/ps/2004pdf/04-ID-07-final.pdf*)
Taken from CDC. Revised surveillance case definitions for HIV infection among adults, adolescents, and children aged <18 months and for HIV infection and AIDS among children aged 18 months to <13 years—United States, 2008. MMWR 2008:57 (RR10); 1–8. Available at: *http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5710a1.htm*

BOX 22.1

Acquired Immunodeficiency Syndrome (AIDS)-Defining Conditions

- Bacterial infections, multiple or recurrent[a]
- Candidiasis of bronchi, trachea, or lungs
- Candidiasis of esophagus[b]
- Cervical cancer, invasive[c]
- Coccidioidomycosis, disseminated or extrapulmonary
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis, chronic intestinal (>1 month's duration)
- Cytomegalovirus (CMV) disease (other than liver, spleen, or nodes), onset at age >1 month
- CMV retinitis (with loss of vision)[b]
- Encephalopathy, HIV related
- Herpes simplex: chronic ulcers (>1 month's duration) or bronchitis, pneumonitis, or esophagitis (onset at age >1 month)
- Histoplasmosis, disseminated or extrapulmonary
- Isosporiasis, chronic intestinal (>1 month's duration)
- Kaposi sarcoma[b]
- Lymphoid interstitial pneumonia or pulmonary lymphoid hyperplasia complex[a,b]
- Lymphoma, Burkitt (or equivalent term)
- Lymphoma, immunoblastic (or equivalent term)
- Lymphoma, primary, of brain
- *Mycobacterium avium* complex or *Mycobacterium kansasii*, disseminated or extrapulmonary[b]
- *Mycobacterium tuberculosis* of any site, pulmonary,[b,c] disseminated,[b] or extrapulmonary[b]
- *Mycobacterium*, other species or unidentified species, disseminated[b] or extrapulmonary[b]
- *Pneumocystis jiroveci* pneumonia[b]
- Pneumonia, recurrent[b,c]
- Progressive multifocal leukoencephalopathy
- *Salmonella* septicemia, recurrent
- Toxoplasmosis of brain, onset at age >1 month[b]
- Wasting syndrome attributed to HIV

[a]Only among children aged <13 years. (CDC. 1994 Revised classification system for human immunodeficiency virus infection in children less than 13 years of age. MMWR 1994;43[No. RR-12].)
[b]Condition that might be diagnosed presumptively.
[c]Only among adults and adolescents aged ≥13 years. (CDC. 1993 Revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. MMWR 1992;41[No. RR-17].)
Taken from CDC. Revised surveillance case definitions for HIV infection among adults, adolescents, and children aged <18 months and for HIV infection and AIDS among children aged 18 months to <13 years—United States, 2008. MMWR 2008:57 (RR10); 1-8. Available at: *http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5710a1.htm*

Therapy

Therapy for HIV focuses on reducing viral load, restoring and/or preserving immune function, improving quality of life, and reducing morbidity and death. Lower viral loads are associated with nonprogression of the disease; higher viral loads are associated with increased probability of clinical manifestations such as infections and other conditions and increased risk of transmission of the virus. Most regimens consist of several different types of drugs including antiretrovirals, protease inhibitors, entry/fusion inhibitors, and integrase inhibitors (NIAID, 2011). Each drug's action is directed toward interfering with a step in the replication of the virus or with entry of the virus into an uninfected cell. Collectively, the therapy is known as highly active antiretroviral therapy or HAART. Resources for researching specific drugs and their applications and side effects can be found in the Media Menu at the end of this chapter and online at thePoint. Therapy for HIV has improved to the point that in many cases the infection, while not eliminated, is suppressed to such a degree that the disease becomes more of a "chronic" condition that requires medical management for the lifetime of the individual. Opportunistic infections and other diseases associated with HIV infection are treated separately from the HIV infection.

Oral Manifestations of HIV

Oral lesions are often the first indicators of a potential systemic illness, and as a result, oral health care providers are in a unique position to provide initial intervention, diagnosis, and treatment of HIV-related illnesses. Although the overall incidence of oral manifestations related to HIV infection has decreased with the use of HAART (Greenspan et al., 2004; Ives et al., 2001; Patton et al., 2000; Ceballos-Salobrena et al., 2000), oral lesions remain a significant cause of morbidity and mortality in HIV-**seropositive** patients. Factors that increase the probability of developing oral lesions include CD4 counts less than 200 cells/mm^3, viral load more than 3,000 copies/mL, xerostomia, poor oral hygiene, and smoking (Butt et al., 2007; Sroussi et al., 2007; Tappuni et al., 2001; Aquirre et al., 1999). The following discussion covers the most commonly encountered oral manifestations seen in association with HIV infection.

Candidiasis

Candidiasis is a common intraoral condition that may be the first manifestation of potential HIV infection and is often a recurrent problem in HIV/AIDS patients (Thompson et al., 2010; Silverman et al., 1996). Intraoral candidiasis is most frequently caused by *Candida albicans*; however, other species may be involved including *C. tropicalis*, *C. glabrata*, *C. krusei*, and *C. parapsilosis* (Badiee et al., 2010; Redding et al., 2000). Oral lesions associated with candidiasis can be classified as pseudomembranous, hyperplastic, or atrophic (erythematous), and may manifest as chronic angular cheilitis.

FIGURE 22.1. Pseudomembranous candidiasis. Yellow, curd-like lesions that rub off easily.

The pseudomembranous form is characterized by creamy yellow or white, curd-like deposits that may be easily wiped away, exposing red or bleeding surfaces beneath (Fig. 22.1). Patients may complain of a burning sensation or an altered taste sensation, but many patients are asymptomatic. Occasionally, the infection may progress to involve the esophagus, resulting in discomfort, difficulty in swallowing, nausea, chest pain, and weight loss. The hyperplastic form of candidiasis is also white, but the lesions are not easily removed. It occurs as firm white lesions that may be mistaken for hairy leukoplakia when present on the tongue (Fig. 22.2). Erythematous or atrophic candidiasis produces a generalized or patchy erythema that is most frequently observed on the palate and the tongue. Its distribution often follows the pattern of a removable appliance if present (Fig. 22.3). Angular cheilitis affects the corners of the mouth, where patients may complain of cracking, redness, and swelling (Fig. 22.4). Other clinical conditions associated with oral candidiasis include black hairy tongue and median rhomboid glossitis.

The presence of candidiasis can be confirmed through a culture or smear; however, most patients are treated empirically, based on clinical presentation. Esophageal

FIGURE 22.2. Hyperplastic candidiasis. Firm white lesion that is not easily removed.

FIGURE 22.3. Atrophic candidiasis. Erythema following outline of temporary removable partial denture.

candidiasis that is refractory to treatment may require endoscopy to assist in establishing a definitive diagnosis. Topical antifungals are useful in the treatment of patients with oral candidiasis, including both rinses and lozenges or troches. Nystatin is the most common rinse used to manage patients with oral candidiasis, while both nystatin and clotrimazole are available as lozenges. Topical miconazole formulated as a buccal tablet has been shown to be as effective as clotrimazole (Vazquez et al., 2010) while less expensive protocols such as topical application of gentian violet remain in use. Care must be taken when using some topical medications over prolonged periods, because sugar content in these formulations is often high enough to contribute to caries in xerostomic patients. Ketoconazole, fluconazole, and itraconazole are the most common systemic antifungals used to treat oral candidiasis; however, resistance is possible if used over prolonged periods of time (Pienaar et al., 2010). Resistant cases may respond to posaconazole (Skiest et al., 2007) or amphotericin B administered orally or intravenously (Queiroz-Telles et al., 2001; Menon et al., 2001; Vazquez, 2000; Linpiyawan et al., 2000; Powderly et al., 1995; Redding et al., 1992). Angular cheilitis is often managed with nystatin ointment or cream applied directly to the corners of the mouth (Sharon et al., 2010). Patients with removable appliances such as dentures, nightguards, or orthodontic retainers should be advised to treat both their mouth and their appliance to reduce the chance of reinfection (Jose et al., 2010; Perezous et al., 2005).

Hairy Leukoplakia

Oral hairy leukoplakia was originally described in 1984. It manifests as nonpainful, bilateral white plaques on the lateral borders of the tongue (Fig. 22.5). The lesions have a corrugated or shaggy appearance with accentuated vertical folds, resulting in a relatively distinct clinical appearance. Ectopic lesions have been observed on the labial and buccal mucosa. Hairy leukoplakia is usually diagnosed by clinical appearance; however, the differential diagnosis must include hyperplastic candidiasis, frictional or smoking-related hyperkeratosis, lichen planus, and benign migratory glossitis (Scully et al., 1999). Hairy leukoplakia is associated with Epstein-Barr virus, a member of the herpesvirus family and, as a result, fails to respond to antifungal therapy (Mendoza et al., 2008). Lesions may be observed in any immunocompromised patient, including those with HIV/AIDS, solid organ transplant patients, and patients using medications designed to suppress the immune system (Piperi et al., 2010; Nicolatou et al., 1999; Schmidt-Westhausen et al., 1990).

Hairy leukoplakia is often not treated specifically, and the lesions usually resolve with initiation of antiretroviral therapy for HIV infection. Although patients are most frequently asymptomatic, the presence of oral lesions may be an aesthetic concern. Current treatment modalities include topical application medications including podophyllin, alone or in combination with antiviral agents, and retinoic acid, systemic antivirals, and surgical removal (Moura et al., 2010; 2007; Gowdey et al., 1995; Lozada-Nur & Costa, 1992; Glick & Pliskin, 1990). All of these treatment modalities may fail to predictably prevent recurrence, and as a result, patients often require additional treatment.

FIGURE 22.4. Angular cheilitis. Erythema, cracking, and fissuring of the corners of the mouth.

FIGURE 22.5. Hairy leukoplakia. White lesion on lateral border of the tongue with corrugated surface.

Human Papilloma Virus Lesions

Of the more than 100 human papilloma virus (HPV) types currently identified and capable of causing both dermal and mucosal lesions, approximately 24 are associated with the oral cavity (Terai et al., 1999). Each of these organisms are small DNA viruses that have the ability to infect stratified squamous epithelium and induce proliferative changes that can result in both benign and potentially malignant changes (Eversole, 2000). As a result, some mucosal HPV subtypes have been divided into low-risk wart types (HPV 6 and 11) and high-risk cancer types (HPV 16 and 18). HPV is present in the normal mucosa in approximately one-third of the general population and is shed in the saliva. The modes of transmission include reactivation of latent virus acquired earlier in life, autoinoculation from skin and facial lesions, or sexual transmission. Despite HAART, the incidence of HPV-associated oral warts appears to be increasing (Syrjanen, 2011; King et al., 2002; Greenspan et al., 2001).

Three human types of benign warts related to HPV infection occur in the oral cavity, including verruca vulgaris (HPV subtypes 2 and 4), squamous papilloma (HPV subtypes 6 and 11), and condyloma acuminatum (HPV subtypes 6 and 11) (Syrjanen, 2003; Piattelli et al., 2001). Focal epithelial hyperplasia (referred to as Heck disease in children) is associated with types 13 and 32 and has been described in HIV-infected patients as resulting in multiple nodular lesions (Moerman et al., 2001). Each of these lesions varies slightly in histologic appearance, but all produce epithelial proliferations demonstrating superficial keratinocytes with pyknotic nuclei surrounded by clear zones (koilocytes), a classic microscopic feature of HPV infection.

Oral lesions most commonly related to HPV infection manifest as singular or, more frequently, multiple papillomas or wart-like lesions that are nonpainful (Fig. 22.6). The lesions can be nodular with a smooth surface, may possess an irregular or cauliflower appearance, or may be shaggy lesions with finger-like projections. The lesions are most commonly seen on the nonkeratinizing mucosa, including the labial mucosa, soft palate, floor of the mouth, and lateral borders of the tongue. Oral condyloma acuminatum is a sexually transmitted disease in which HPV appears to be a major etiologic agent (Newland, 2000). Lesions occur 1 to 3 months following exposure and are often accompanied by anogenital involvement. HIV-positive subjects are much more likely to have an oral HPV infection, to be infected with more than one type of HPV, and to be infected with a high-risk type of HPV than HIV-negative subjects (Syrjanen, 2011; Kreimer et al., 2004). The prevalence of oral warts in HIV-positive patients is estimated to be between 1 and 4%.

High-risk HPV subtypes such as HPV 16 are associated with cervical, vulvar, vaginal, penile, and anal cancer, as well as certain head and neck cancers (Grulich et al., 2010; D'Souza et al., 2007; Parkin, 2006). HPV infection is associated with 20 to 25% of squamous cell carcinomas of the head and neck, primarily oropharyngeal cancers. Approximately, 80 to 90% of oropharyngeal carcinomas carry HPV 16; however, a definite causal relationship has not been established (Kumaraswamy et al., 2011; Zhao et al., 2009).

FIGURE 22.6. Human papillomavirus lesions. Multiple wart-like lesions within the oral cavity.

Treatment of patients with wart-like oral HPV lesions may include surgical removal, cryotherapy, laser ablation, or electrocautery. In addition, keratolytic agents applied topically, such as podophyllin resin and intralesional injections of interferon or cidofovir, have shown therapeutic benefit (Lipke, 2006; Lozada-Nur et al., 2001; Eversole, 2000; Ishida and Ramos-e-Silva, 1998). Recurrence following removal as well as the development of new lesions is likely, and patients may require repeated episodes of treatment. Vaccination against HPV 6, 11, 16, and 18 is currently available for both females and males to prevent cervical cancer and genital warts (Lu et al., 2011; Giugiano et al., 2011). The influence of HPV vaccines on other types of cancer including those affecting the head and neck has yet to be established.

Malignancies or Neoplastic Lesions

Kaposi sarcoma (KS) is the most common AIDS-associated neoplasia and remains a significant cause of morbidity and mortality in HIV-infected patients (Chu et al., 2010). The lesions manifest as an angiomatous malignancy of the skin and mucosa that may spread to the lungs, liver, or

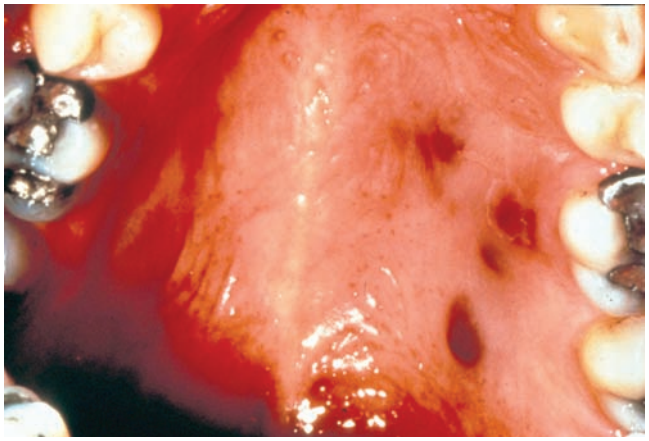


FIGURE 22.7. Kaposi sarcoma. Flat, nonpainful purple lesion on the palate.

FIGURE 22.9. Non-Hodgkin lymphoma. Large mass involving mandibular anterior gingiva.

gastrointestinal tract. It appears to be associated with a sexually transmitted virus (human herpesvirus 8). The oral cavity is the first site of involvement in 20 to 70% of cases, and the hard palate and gingiva are the most frequently affected sites (Kalpidis et al., 2006; Gorsky & Epstein, 2000). Early lesions occur as nonpainful, purple-to-red macules that may be focal or diffuse and are easily overlooked (Fig. 22.7). As the lesions progress, they may become nodular and exophytic, interfering with function and/or aesthetics (Scully et al., 1991) (Fig. 22.8). Along with initiation of antiretroviral therapy, medical management of patients with KS may include the use of interferon alfa, chemotherapy, and radiation therapy (Di Lorenzo et al., 2007). Oral lesions are often managed with laser excision, cryotherapy, or intralesional injections with vinblastine (Flaitz et al., 1995; Epstein et al., 1989).

Non-Hodgkin lymphoma is another neoplastic condition seen more frequently in immunocompromised patients (Simard et al., 2010). Plasmablastic lymphoma is a rare form of non-Hodgkin lymphoma that is strongly associated with HIV infection. Oral lesions occur in approximately 4% of HIV patients with non-Hodgkin lymphoma, and the mouth may be the first site of involvement (Navarro et al., 2008; Desai et al., 2007). Patients present with rapidly growing, painful masses that are often ulcerated and most frequently appear on the gingiva or palate (Lozada-Nur et al., 1996) (Fig. 22.9). Diagnosis is confirmed through biopsy and histologic evaluation, and patients are generally referred for medical management. Therapy often includes the use of radiation or chemotherapy, necessitating evaluation and stabilization of dental needs prior to treatment.

FIGURE 22.8. Kaposi sarcoma. Exophytic mass that interferes with function.

Oral Ulcerations

Oral ulcerations are common in the immunocompromised patient, and severity, response to therapy, and the propensity for recurrence may be different from that in the general population (Kerr & Ship, 2003; MacPhail & Greenspan, 1997). The most common ulcerations manifest primarily as recurrent aphthae and herpes simplex virus type 1 lesions (MacPhail et al., 1992). Substantially less common are ulcerations related to cytomegalovirus (CMV) infection, fungal infections such as histoplasmosis and cryptococcosis, and bacterial infections such as tuberculosis and syphilis (Guttal et al., 2010; Mahajan et al., 2007). Oral ulcerations may also be related to HIV-related neutropenia. Because the clinical appearance may be similar in many of these lesions, biopsy and/or culture of persistent, atypical-appearing ulcerations may be indicated to arrive at a definitive diagnosis and appropriate treatment.

Recurrent aphthae are common oral lesions affecting approximately 10 to 20% of the general population (Ship et al., 2000). Most patients report a history of recurrent lesions developing prior to the age of 30, and a possible familial predisposition exists. A potential systemic etiology should be considered in patients who spontaneously develop chronic, severe episodes that do not respond to therapy. Aphthae are classified according to size and duration into three groups: minor aphthae, major aphthae, and herpetiform aphthae. Minor aphthae are small lesions (<5 mm in diameter) that occur as single or multiple ulcerations. Minor aphthae generally affect the mobile mucosa (tongue,

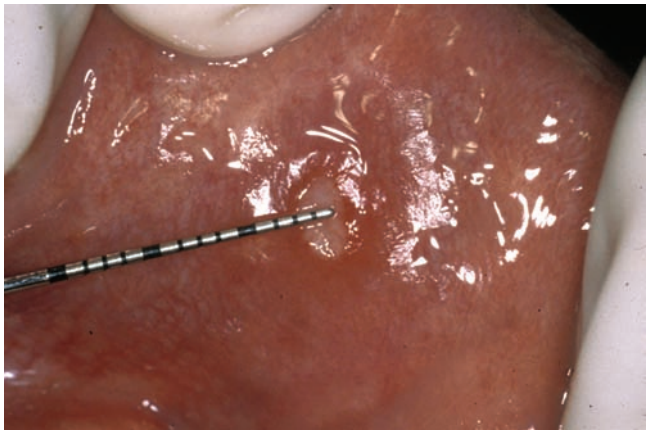


FIGURE 22.10. Minor aphthous ulcer. Small ulceration with fibrinous coating and red halo.

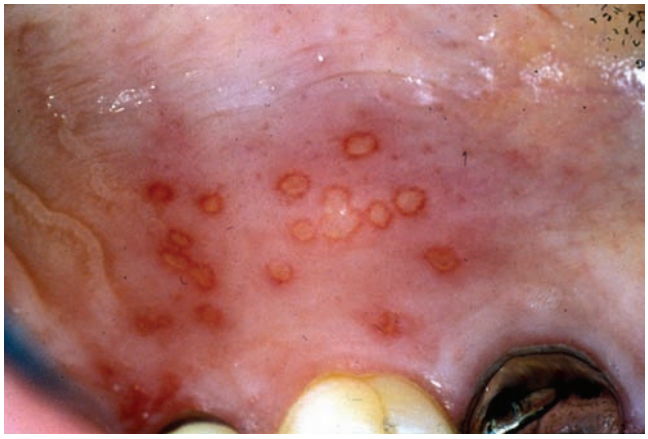


FIGURE 22.12. Recurrent herpetic stomatitis. Multiple small ulcerations on hard palate.

floor of mouth, soft palate, and buccal/labial mucosa) and manifest as superficial erosions with a fibrinous covering, often surrounded by a red halo (Fig. 22.10). The lesions persist for 7 to 14 days and can cause significant discomfort. Major aphthae are characterized by larger, painful ulcerations that persist for up to 6 weeks and initially heal with scarring (Fig. 22.11). Herpetiform aphthae occur as crops of small ulcers that coalesce and may be mistaken for herpes simplex virus lesions.

Aphthae respond well to topical steroid therapy, including the use of fluocinonide, clobetasol, and betamethasone; however, patients should be closely monitored for subsequent development of candidiasis (Scully et al., 2003; Eisen & Lynch, 2001; Muzio et al., 2001; MacPhail et al., 1992). Other topical medications for the treatment of aphthae include tetracycline, chlorhexidine, and amlexanox (Rodriquez et al., 2007; Porter & Scully, 2005; Khandwala et al., 1997). Topical anesthetics and coating agents provide temporary pain relief along with chemical cautery and laser ablation (De Souza et al., 2010). Intralesional injections with triamcinolone may be useful for isolated persistent lesions, and systemic steroid therapy including prednisone is useful for patients with severe outbreaks. Systemic thalidomide has also shown therapeutic efficacy in patients with recalcitrant lesions (Shetty, 2007; Calabrese & Fleischer, 2000; Jacobson et al., 1997).

FIGURE 22.11. Major aphthous ulcer. Large ulceration with indurated borders.

Recurrent herpetic stomatitis is characterized by multiple, small vesicles, which quickly rupture to form ulcerations. These ulcerations often coalesce, creating a larger lesion that is associated with significant discomfort (Fig. 22.12). Though the lesions traditionally affect primarily the palate and attached gingiva or the vermillion border, in patients who are significantly immunosuppressed, lesions may involve any mucosal surface. Recurrent herpetic stomatitis is caused by herpes simplex virus type 1, and most lesions respond to systemic antiviral therapy including acyclovir, valacyclovir, or famiciclovir (Arduino & Porter, 2006; Itin & Lautenschlager, 1997; Flaitz et al., 1996). Topical therapy with penciclovir may be useful in some patients (Femiano et al., 2001). Intravenous administration of foscarnet may be indicated in patients whose lesions are recalcitrant to therapy with acyclovir (Fatahzadeh et al., 2007).

In contrast to recurrent aphthous and recurrent herpetic stomatitis, oral ulcerations associated with CMV are more frequently seen in patients with AIDS nearing the advanced stages of the disease. Approximately 50% of the general population and 90% of patients with HIV are carriers of the virus that causes CMV-related disease. When HIV weakens a patient's immune defenses, CMV can attack several parts of the body, most frequently the retina, colon, and esophagus. Within the oral cavity, CMV lesions occur as persistent, painful oral ulcerations with irregular or punched-out borders and covered by a pseudomembrane (Doumas et al., 2007; Syrjanen et al., 1999; Reichart, 1997; Firth et al., 1994; Jones et al., 1993; Schubert et al., 1993). Diagnosis frequently requires a viral culture or biopsy of the lesion along with immunohistochemistry. Treatment is best managed by physicians and may include the use of ganciclovir, foscarnet, and cidofovir (Salmon-Ceron, 2001; Naesen & DeClercq, 2001).

Histoplasmosis and cryptococcosis are both fungal infections that may manifest within the oral cavity as persistent ulcerations. Histoplasmosis is a fungal infection

caused by the organism *Histoplasma capsulatum*, in which over 30% of patients demonstrate oral lesions (Epifanio et al., 2007; Gomes Ferreira et al., 2001; Piluso et al., 1996; Chinn et al., 1995). The lesions occur most frequently on the gingiva, tongue, buccal mucosa, and soft palate and manifest as granulomatous-appearing ulcerations with indurated borders covered by a nonspecific gray membrane. Cryptococcosis is another deep fungal infection, caused by the organism *Cryptococcus neoformans*, which can manifest intraorally as a nonspecific ulceration (Iatta et al., 2009; Schmidt-Westhausen et al., 1995). Both of these conditions require assessment for systemic disease and are best managed by physicians. Treatment frequently includes the use of systemic antifungals including ketoconazole, fluconazole, itraconazole, or amphotericin B.

Other, more infrequent causes of intraoral ulcerations are bacterial infections including tuberculosis and primary syphilis (Kakisi 2010; Alam et al., 2000; Anil et al., 2000). Once identified through culture or biopsy, patients require referral to a physician for a medical evaluation and treatment.

Periodontal Diseases

Chronic gingivitis and periodontitis remain as the most common forms of periodontal disease affecting the general population as well as HIV-infected patients (Kroidl et al., 2005). Although less frequently encountered, three atypical forms of periodontal disease have been associated with HIV infection: linear gingival erythema, necrotizing ulcerative gingivitis, and NUP (Mataftsi et al., 2011; Narani & Epstein, 2001; Ryder, 2000; Grbic & Lamster, 1997).

Linear gingival erythema generally manifests as a persistent, generalized 2- to 3-mm band of erythema involving the marginal and papillary gingiva. The lesions are generally nonpainful and can range in appearance from a distinct band of bright red gingiva to more subtle and diffuse erythema (Fig. 22.13). Occasionally, lesions extend into the attached gingiva and manifest as petechia-like patches that are often accompanied by bleeding. A distinguishing feature of linear gingival erythema is that it is often refractory to treatment and persists despite both adequate oral self care and periodontal debridement. Treatment includes efforts to improve oral hygiene, periodontal debridement, the use of topical chemotherapeutic agents such as chlorhexidine rinses, and supportive periodontal therapy at shorter intervals to monitor progression. Although putative periodontal pathogens are most commonly isolated from areas of linear gingival erythema, a candidal origin has been suggested (Aas et al., 2007). As a result, antifungals are occasionally useful in nonresponsive patients.

FIGURE 22.14. Acute necrotizing gingivitis. Loss of papillae in mandibular anterior region with associated attachment loss.

Necrotizing ulcerative gingivitis is characterized by rapid onset of periodontal destruction, including marked necrosis and ulceration of the marginal and papillary gingiva (Holmstrup & Westergaard, 1998). Patients generally experience severe pain, spontaneous bleeding, and a distinct oral malodor. Destruction of the interdental tissue results in open interproximal areas and soft tissue craters, making future oral self-care more difficult (Fig. 22.14). Lesions may occur throughout the dentition; however, the mandibular incisor and maxillary molar regions are most commonly affected.

NUP occurs as the disease progresses to involve the underlying bone and supporting tissues (Reznik, 2005) (Fig. 22.15). It has been reported in 0 to 5% of the HIV-seropositive population and is associated with advanced

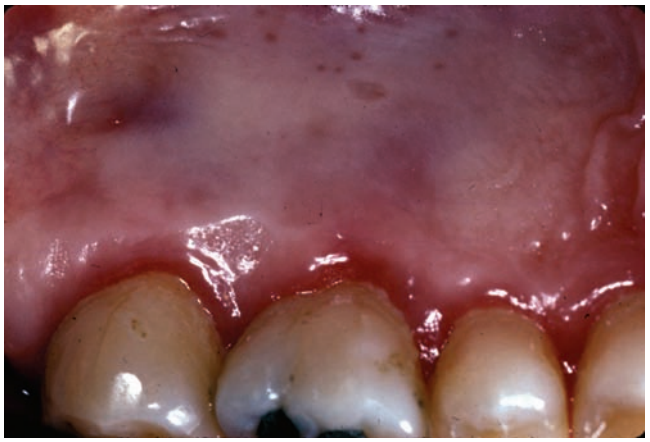


FIGURE 22.13. Linear gingival erythema. Marginal and papillary erythema that does not resolve despite periodontal debridement.

FIGURE 22.15. Acute necrotizing periodontitis. Infection resulting in exposure of bone.

immune suppression and CD4 counts often below 100/mm^3. Patients often complain of deep bone pain as soft tissue destruction occurs very rapidly, exposing underlying alveolar bone (Feller et al., 2006; Novak, 1999). The exposed bone quickly becomes necrotic and may eventually slough away as a sequestrum or require surgical debridement. Alveolar ridge defects are common following NUP, and tooth loss is common.

Pain control and management of infection through sequential episodes of periodontal debridement and antimicrobial therapy are cornerstones of treatment. Therapy often begins with gentle debridement performed at frequent intervals, followed by more thorough periodontal instrumentation. Topical antimicrobials including chlorhexidine and povidone–iodine are useful as rinses or for subgingival irrigation. Systemic antibiotics are indicated, especially if signs of systemic involvement are present, including swelling and lymphadenopathy, or if bone exposure is apparent. Metronidazole has been shown to be particularly effective in the management of patients with NUP; however, care must be taken to monitor for potential secondary candidiasis (Robinson, 1997). In addition, patients must be advised to avoid the use of alcohol during metronidazole therapy. Alternative systemic antimicrobials include amoxicillin/clavulanate and clindamycin. Healing is often dramatic, with a rapid reduction in erythema and ulceration. However, oral hygiene remains complicated by residual soft tissue craters and open interproximal spaces. The need for regular and frequent supportive periodontal care is of extreme importance in patients with a history of NUP (Hofer et al., 2002).

Salivary Gland Disease and Xerostomia

Patients with HIV infection may present with enlargement of the salivary glands due to several factors, including cyst formation, infection, malignancy, and xerostomia (Fig. 22.16). Enmeshed within the intraparotid lymph nodes formed during embryonic development, salivary gland tissue may demonstrate epithelial proliferation leading to lymphoepithelial cyst formation (Patel & Mandel, 2001; Mandel & Hong, 1999). The swelling is usually bilateral and nonpainful, and resolution following initiation of antiretroviral therapy may occur (Syebele & Butow, 2011). Although specific treatment is not necessary in many cases, patients may seek therapeutic alternatives to address aesthetic concerns. Care must be taken to rule out other conditions such as infection (CMV) and neoplasias (lymphoma) (Bishop & Westra, 2010). As a result, radiographic imaging of the glands, fine needle biopsy, and immunohistochemistry may be indicated (Michelow et al., 2011).

Oral ranulas and mucoceles are more frequently observed in HIV-infected patients and may be the presenting symptoms for which patients seek dental care (Syebele & Butow, 2010).

Xerostomia is a common complaint in patients with HIV/AIDS (Younai et al., 2001; Navazesh et al., 2000).

FIGURE 22.16. Salivary gland swelling due to lymphoepithelial cyst formation in parotid gland.

Salivary hypofunction can be related to early HIV infection (Lin et al., 2003), and xerostomia may be a side effect of medications used to manage HIV-positive patients (Diz Dios & Scully, 2002). Patients may experience an inability to eat comfortably, and the oral tissues may be easily traumatized, resulting in nonspecific ulcerations. Candidiasis is more common in xerostomic patients, and caries can become a significant concern. Patients should be encouraged to increase their intake of water throughout the day and may find relief through the use of salivary substitutes or oral lubricants. Systemic medications such as pilocarpine and cevimeline increase secretions and may be useful in patients without significant gastrointestinal problems. Home fluoride therapy as well as regular professional dental care are essential in reducing the risk of caries and periodontal disease.

SUMMARY

- HIV is a retrovirus (RNA) from the Lentivirus group characterized by having a prolonged latency period between infection and manifestation of symptoms.
- Up to 70% of infected individuals experience flu-like symptoms called the acute primary infection which occurs 2 to 4 weeks after infection and resolves spontaneously about 2 to 3 weeks later.

- Seroconversion occurs when antibodies to HIV are detected in the blood. Before seroconversion, blood tests to detect HIV RNA are used to identify those with the infection. After seroconversion, tests that identify the antibodies to HIV are utilized to diagnose HIV infection.
- HIV has a clinical latency period of varying lengths (depending on the individual). The latency period is usually asymptomatic but may present with PGL.
- Manifestations of the later stages of HIV infection are collectively known as AIDS which is characterized by the presence of any number of opportunistic infections or conditions associated with a compromised immune system.
- Therapy for HIV is directed toward reducing viral load, maintaining immune system function, improving quality of life, and reducing morbidity and mortality. Patients are prescribed combinations of drugs in regimens referred to as HAART.
- Although the incidence of oral lesions has decreased with HAART, oral lesions continue to occur frequently and are often the early manifestations of patients with HIV infection.
- Many intraoral conditions associated with HIV infection can be managed well in the dental office.
- Candidiasis, in any of its forms, is a common infection associated with HIV. These infections are often recurrent and resistant to therapy. Occasionally the infection will involve the esophagus. Initial therapy consists of topical antifungals followed by systemic antifungals for resistant cases.
- Oral hairy leukoplakia (Epstein-Barr virus) is associated with immunosuppression and is characterized by bilateral white plaques on the lateral borders of the tongue (or other surface). These lesions usually resolve when antiretroviral therapy begins.
- The incidence of HPV-associated oral warts is increasing despite HAART. HIV-positive individuals are much more likely to have an oral HPV infection, to be infected with more than one type of HPV, and to be infected with a high-risk type of HPV than HIV-negative individuals. Treatment consists of surgical or other form of removal, and recurrence and formation of new lesions are common.
- KS (human herpesvirus 8) is the most common AIDS-associated neoplasm. The oral cavity is the first site of involvement in 20 to 70% of cases, and the hard palate and gingiva are the most frequently affected sites. Lesions are treated with laser excision, cryotherapy, or intralesional injections of vinblastine.
- Non-Hodgkin lymphoma is also seen more in immunocompromised persons. Oral lesions are referred for medical treatment with radiation or chemotherapy.
- Oral ulcerations are common and may be associated with recurrent aphthae, herpes simplex type 1, and less frequently CMV, fungal infections, and bacterial infections.
- Oral recurrent aphthae respond well to topical steroids; recurrent herpetic stomatitis responds to systemic antiviral therapy.
- Ulcers caused by CMV occur more frequently during the more advanced stages of AIDS and are best managed by physicians.
- Bacterial infections and deep fungal infections should be referred for medical evaluation and treatment.
- While chronic gingivitis and periodontitis are the most common forms of periodontal disease seen in HIV-positive patients, there are three atypical forms of periodontal disease that are also seen: linear gingival erythema, necrotizing ulcerative gingivitis, and NUP.
- Linear gingival erythema is painless and resistant to treatment even if treatment and oral self-care is adequate.
- NUP causes deep bone pain and often results in alveolar bone necrosis and sequestration.
- Salivary gland disease is not uncommon in HIV infection and usually presents bilateral enlargement of the glands which may resolve when HAART is initiated. Other etiologies such as neoplasms or infections should be ruled out.
- The need for routine comprehensive dental care for HIV-positive patients is critical.

CHAPTER REVIEW

Case Study 22.1

A 32-year-old male was scheduled for a recall dental hygiene appointment and contacted the office to be seen sooner because of severe gingival pain. He reported his problem began 1 week ago when he noticed bleeding, pain, and ulceration of the gingiva in the mandibular anterior region along with bad breath (Fig. 22.17). The patient's record reflected that he was diagnosed as being HIV positive 7 years ago, at which time he started antiretroviral medications (HAART).

1. Describe the clinical changes shown in the intraoral photograph?
2. What is the most likely condition represented in the photograph?
3. What questions might you want to ask this patient regarding his history?
4. List the possible treatment options for this patient.

For answers and additional review activities, log in to **thePoint.lww.com**

FIGURE 22.17.

Case Study 22.2

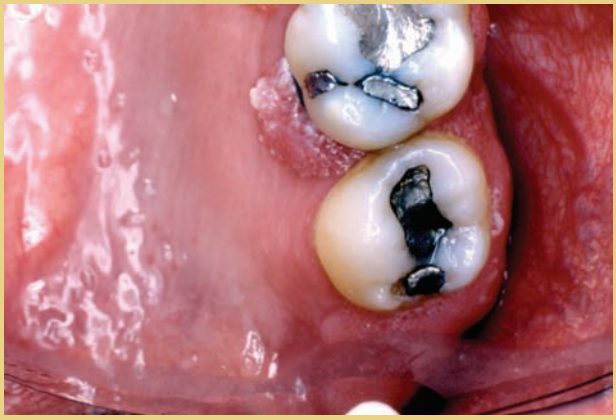
A 48-year-old Latino male presents with the following positive findings on his medical history:

- HIV positive since 1987
- Hepatitis B and C
- Hypertension
- Hyperlipidemia
- Previous treatment for depression
- Current medications
  - Viread (Tenofovir)
  - Epivir (Lamivudine), 3TC
  - Agenerase (Amprenavir)
  - Kaletra (Lopinavir + Ritonavir)
  - Lipitor (Atorvastatin)
  - Quinapril

The patient does not know what his current immune status is so he is sent for blood tests. Laboratory test values are as follows:

- CD4 = 41
- Viral load = 15,000

A



B

C

FIGURE 22.18.

The patient has multiple dental concerns he would like addressed (refer to the clinical photographs in Figures 22.18A-C):

- Xerostomia
- Multiple and recurrent HPV lesions
- History of NUP resulting in loss of lower front teeth
- Restorative needs
  - Multiple carious lesions
  - Missing teeth

1. This patient's problem with caries is related in part to his xerostomia. What are the current options available to manage xerostomia and caries in order to prevent further tooth loss?
2. How can his recurrent HPV lesions be managed so that a removable partial denture can be fabricated?
3. What measures can be taken to prevent further tooth loss due to NUP?

Critical Thinking Activity

1. Testing for HIV using a sample of the patient's saliva has been possible since 2004. Do you think testing should be done routinely in the general dental practice? Who would report the results to the patient and how?

Portfolio Possibility

- Prepare a resource list of web sites, community agencies, government agencies, etc. where you can access HIV-specific information you might require for assessing and treating a patient who is HIV positive. Also include in your list local clinics/practitioners offering specialized care for cases beyond the scope of the general dental office in case you need to make a referral. Make sure you include information from your local area that you can share with your patient, such as outreach organizations, support groups, community sources of funds for dental care, etc.

Media Menu

Web Sites

HIVdent: The Internet's HIV/AIDS Oral Healthcare Resource—Excellent reference for all things dental and current drug information)
www.hivdent.org

HIV InSite from University of California, San Francisco—Good medication references under "Knowledge Base," Antiretroviral Therapy:
www.hivinsite.org

Evaluation Center for HIV and Oral Health (ECHO)
http://www.hdwg.org/echo/

National Institutes of Health: AIDSinfo—Excellent drug reference and treatment guidelines
http://www.aidsinfo.nih.gov/

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Take advantage of additional online resources to help you study and ace your exams!

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- Additional case studies and answers
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- Expanded Media Menu with direct links to related Web sites and multimedia resources
- Supplemental references

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CHAPTER 22 **LESION/CONDITION SUMMARY TABLE**

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Acute Primary Infection	Human immunodeficiency virus	Occurs in up to 70% of infections, coincides with severe drop in CD4 T cells, associated with initial infection	Flu-like symptoms, fever, fatigue, rash, sore throat, lymphadenopathy	Not applicable	Should be reported to physician to aid in diagnosis of primary infection, symptoms will resolve spontaneously within 2–3 weeks	Report any flu-like symptoms after a significant blood or body fluid exposure to your physician, discuss patient's need to report symptoms to physician as well as prevention strategies if patient is at risk for HIV
Acquired Immunodeficiency Syndrome	Human immunodeficiency virus	Syndrome occurs in the late stages of HIV infection when the immune system is significantly compromised and no longer able to compensate for loss of CD4 T cell function.	Characterized by the presence of a variety of opportunistic infections, death is caused by one or more of these conditions rather than HIV itself.	Not applicable	Antiretrovirals (HAART) including protease inhibitors, entry/fusion inhibitors, integrase inhibitors. Treatment for AIDS-related opportunistic infections/ conditions.	Obtain a thorough medical/dental/ medication history and determine the patient's immune status (CD4 T cell count) prior to any treatment. Research side effects of HIV medications, potential dental side effects and interactions with medications used in dentistry. Discuss caries and periodontal disease prevention for patients at increased risk.
Candidiasis (see Chapter 14)	*Candida albicans* or other *Candida* species	Common opportunistic infection	May manifest as any of the four forms: pseudomembranous, hyperplastic, atrophic, or angular cheilitis	Presence of hyphae on smear or positive culture	Topical and systemic antifungal medications, treatment of removable appliances to prevent reinfection.	Patients with recurrent infections should be evaluated by their physician for immune status, topical medications may have high sugar contents and prolonged use will increase caries risk, assess patient for caries risk and take preventive measures
Hairy Leukoplakia (see Chapter 14)	Epstein-Barr virus	May be seen in any patient with a compromised immune system	Nonpainful bilateral white plaques on the lateral borders of the tongue, corrugates, shaggy appearance with accentuated vertical folds, may also be found rarely on other mucosal surfaces	Not applicable	Usually resolves with HAART, often responds to topically applied podophyllin, may be surgically removed, lesions tend to recur	Often confused with benign migratory glossitis, monitor for recurrence
Human Papilloma Virus (see Chapter 16)	HPV-24 different types associated with oral infection	Lesions develop 1–3 months after exposure, infection also results from autoinoculation from existing lesions, sexual transmission, reactivation of previous infection	Single or multiple papillary or wart-like growths may be nodular with a smooth surface or rough and cauliflower-like, usually seen on nonkeratinized tissues	Epithelial proliferations demonstrating superficial keratinocytes with pyknotic nuclei surrounded by clear zones (koilocytes)	Surgical removal, cryotherapy, laser ablation, electrocautery, topical keratolytic agents and intralesional injections of interferon, etc.	High risk HPV types are associated with 20–25% of head and neck squamous cell carcinomas, vaccines to prevent HPV are available for both boys and girls and should be given prior to sexual activity or puberty
Kaposi Sarcoma (see Chapter 13)	Associated with sexually transmitted human herpes virus 8	Neoplasm of the tissues that form blood vessels, found on skin and mucous membranes, lungs, liver, and GI tract may be affected	Often seen in the oral cavity first (hard palate, gingiva), early lesions nonpainful, purple-to-red macules, lesions may become nodular and exophytic, interfere with function or aesthetics	Not applicable	Oral lesions may be treated with laser excision, cryotherapy, intralesional injection with vinblastine Systemic involvement managed medically with radiation of chemotherapy	Careful observation during the oral examinations is essential because small lesions may be easily over looked
Non-Hodgkin Lymphoma (see Chapter 9)	Unknown/HIV infection is associated with a very high risk of these neoplasms, related to immunosuppression	Neoplasm of B or T lymphocytes affecting organs and tissues associated with the lymphatic system	HIV-associated lymphomas occur frequently in the oral cavity and manifest as rapidly growing, painful, often ulcerated, masses on the hard palate or gingiva	Not applicable	Lesions require medical management consisting of radiation and/or chemotherapy	Patients will need evaluation and treatment of dental needs prior to beginning cancer therapy, confirm immunologic status adequate following cancer treatment, monitor for recurrence

CHAPTER 22 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Aphthous Ulcers (see Chapter 12)	Idiopathic, autoimmune, other systemic condition	Usually affects the moveable mucosa	All 3 types of aphthae are seen, and recurrent, severe episodes are not uncommon in HIV infection	Not applicable	Topical steroids, other topical medications such as tetracycline and chlorhexidine, systemic steroids may be necessary for resistant lesions and systemic thalidomide has shown to be effective in some cases Topical anesthetics are helpful for pain control.	Severe and recurrent aphthous ulcers may present in HIV-positive patients. Resistant oral ulcers should be biopsied to determine exact etiology and appropriate treatment
Herpes Simplex Lesions (see Chapter 11)	Human herpes virus	Initial infection with the virus or reactivation of latent virus	Lesions may affect any mucosal surface in immunocompromised patients, severe episodes may occur	Not applicable	Systemic and/or topical antiviral therapy, intravenous foscarnet for resistant cases	Contact with lesions can result in autoinoculation and viral transmission; provide patient education regarding disease transmission and autoinoculation. Dental patients should be reappointed, if possible, until lesions are healed.
Cytomegalovirus Lesions (see Chapter 6)	Cytomegalovirus (CMV)	Common virus carried by @50% of general population and 90% of HIV-positive patients, opportunistic disease affecting individuals with a compromised immune system, seen more in late stages of AIDS	Often affects the retina, colon, and esophagus; when it occurs in the mouth, it presents as persistent, often large, ulcerations with irregular margins and covered with a pseudomembrane	Not applicable	Medical management consisting of antiviral medications	May be confused with aphthous ulcers, any persistent ulcer should be biopsied to determine exact cause and most appropriate treatment
Linear Gingival Erythema	Usual periodontal pathogens, possibly Candida species	Distinguishing feature is that the condition is often resistant to therapy and may continue even with periodontal therapy and good oral hygiene care	Nonpainful distinct band of bright red along the free gingival margin or more diffuse erythema, may extend into attached gingiva	Not applicable	Periodontal debridement, topical antimicrobials, improved oral hygiene, more frequent follow-up periodontal appointments, antifungal medications if appropriate	Emphasis on education related to prevention and management
Ulcerative Necrotizing Gingivitis	Usual periodontal pathogens and others	Rapid onset of periodontal destruction, including necrosis and ulceration of marginal and papillary gingiva	Severe pain, spontaneous bleeding, and a distinct oral malodor, may lead to NUP if not controlled	Not applicable	Pain control, gentle periodontal debridement followed by more thorough periodontal instrumentation, topical and systemic antimicrobials, frequent follow-up appointments for monitoring and maintaining periodontium	Emphasis on education related to prevention and management, modify patient self-care instructions to address altered anatomy resulting from disease
Ulcerative Necrotizing Periodontitis	Usual periodontal pathogens and more, associated with advanced immunosuppression and CD4 levels below 100 cells/mm^3	Continued destruction of soft tissues extending into the underlying bone which becomes necrotic and sloughs	Patients complain of deep bone pain, rapid soft tissue destruction continues with frequent exposure of the underlying bone	Not applicable	Pain control, gentle periodontal debridement followed by more thorough periodontal instrumentation, topical and systemic antimicrobials, metronidazole very helpful but monitor for secondary fungal infection, frequent follow-up appointments for monitoring and maintaining periodontium	Emphasis on education related to prevention and management, modify patient self-care instructions to address altered anatomy resulting from disease

CHAPTER 23

Skin Lesions

KEY TERMS

Actinic cheilitis
Actinic keratosis
Acrochordon
Angular cheilitis
Angular stomatitis
Basal cell carcinoma
Comedones
CREST syndrome
Eczema
Ephelides
Erythema multiforme
Favre-Racouchot disease
Graft versus host disease
Impetigo
Keloid
Leishmaniasis
Lichen planus
Lupus
Melanoma
Milia
Nevi
Perlèche
Pityriasis rosea
Poison oak
Psoriasis
Raynaud phenomenon
Rhinophyma
Rosacea
Sarcoidosis
Sclerodactyly
Scleroderma
Seborrheic keratosis
Solar lentigo
Squamous cell carcinoma
Telangiectasia
Urticaria
Vitiligo
Warts
Xanthelasma

LEARNING OUTCOMES

1. List the three major types of skin cancer and discuss the areas that are particularly important to evaluate during your extraoral exam of the patient.
2. Describe the ABCDEs of skin cancer.
3. List and discuss four causes of skin cancer.
4. List five ways to prevent skin cancer.
5. Describe several ways that dental hygienists and dentists can be instrumental in detecting skin cancer.
6. Describe several ways that clinicians can be instrumental in determining the origins of skin lesions and discuss why this is important.
7. List five diseases that have skin lesions as part of the disease state.
8. List five skin lesions that are benign but should be followed, measured, photographed, and documented.
9. List a skin lesion that is caused by *Candida*.
10. Discuss three skin diseases that are a part of a disease process and have oral lesions as well.
11. Describe three benign skin conditions that may be observed clinically but do not pose any major contagion factors.
12. List two diseases that may exhibit skin lesions and may be contagious.
13. Describe vitiligo and discuss the factors that may contribute to the disease state.
14. Discuss graft versus host disease (GVHD) and the skin characteristics that accompany the condition.
15. Compare and contrast comedones, nevi, and moles.
16. List the organs that may be affected by a diagnosis of sarcoidosis.
17. List the characteristics of scleroderma and describe the diseases often associated with scleroderma.

CHAPTER OUTLINE

Malignant Skin Lesions
- Basal Cell Carcinoma, Squamous Cell Carcinoma, and Melanoma

Premalignant Skin Lesions
- Actinic Keratosis
- Actinic Cheilitis

Benign Skin Lesions
- Acrochordon
- Comedones
- Eczema
- Ephelides (Freckles)
- Keloid
- Solar Lentigo
- Milia
- Nevi
- Perlèche (Angular Cheilitis or Angular Stomatitis)
- Pityriasis Rosea
- Poison Oak
- Psoriasis
- Rhinophyma
- Rosacea
- Seborrheic Keratoses
- Urticaria
- Xanthelasma

Diseases Associated with Skin Lesions
- Erythema Multiforme
- Graft versus Host Disease
- Impetigo
- Lichen Planus
- Lupus
- Sarcoidosis
- Scleroderma
- Vitiligo
- Warts
- Leishmaniasis

RELATED CLINICAL PROTOCOLS

#10 Patient Education: UVA/UVB Skin Protection
#11 Patient Education: Oral Cancer Self-Examination
#25 How to Utilize Nutrition Counseling in Practice
#27 Motivational Interviewing for Behavior Change

This chapter provides the student and the practitioner with information related to the extraoral examination. The dental hygienist begins the pathology examination by observing, palpating, and thoroughly examining the external surfaces of the patient. Skin lesions are often evident on the exposed surfaces of the arms, legs, neck, face, and scalp regions. The clinician easily assesses these locations as these areas are often visible during the dental appointment.

In some cases, long-standing lesions may either be premalignant or have changed into a cancerous state.

FIGURE 23.1. Previously removed skin lesions.

Many patients have lesions removed and biopsies performed on a routine basis, since some patients tend to have more moles and develop skin lesions quickly. Patients who have had basal cell and squamous cell carcinoma have higher rates of melanoma and are advised to have any new growth checked frequently. Additionally, a person who has more than 50 moles is at greater risk for any type of skin cancer. The patient in Figure 23.1 has multiple small facial scars from the removal of previous skin lesions on the forehead because of frequent and long-term sun exposure.

The hygienist may be the first person to inquire about a growth and bring it to the attention of the patient. When diagnosed in an early stage, premalignant lesions can be quickly removed and will not cause the patient future problems. Some skin discolorations may appear threatening, and they must be evaluated. A dermatologist is the best person to evaluate such lesions and often must biopsy the tissue to determine the exact nature of the lesion. In addition, some skin lesions may occur because of systemic conditions that are not connected to sun exposure but, rather, result from chronic disease states, radiation, viruses, or an undiagnosed disease that results in skin lesions. The hygienist is in a prime position to assist the patient in getting the treatment needed, in any case. Therefore, all lesions need to be evaluated, and in most cases, when there is any question regarding the lesion, the patient needs to see a dermatologist. Detecting lesions early is of paramount importance to the patient so that early treatment can begin.

The American Academy of Dermatology (AAD, 2012) states that more than 3.5 million skin cancers in more than 2 million people are diagnosed annually and that includes basal cell carcinoma, squamous cell carcinoma, and melanoma. Nationally, there are more new cases of all types of skin cancer each year than the combined incidence of cancers of the breast, prostate, lung, and colon. Skin cancer is the number one cancer seen in men over the age of 50, and it has tripled in women under the age of 40. The risk factors for cancer in general are tobacco use, heavy alcohol use, physical inactivity, a poor diet, unprotected sun exposure including tanning beds, and

TABLE 23.1 **Burn Index**

Skin Type	History of Past Sun Exposures
I	The person is pale, burns very easily, has never tanned, and may have blue or green eyes. The person is usually described as having a "porcelain complexion" with blonde or red hair.
II	The person has a fair complexion and has tanned but gets a minimal tan; may have blue, gray, or green eyes.
III	The person may still be fair complexioned, but burns; will go into a light tan.
IV	The person has a lightly tanned appearance; burns minimally to a moderate brown.
V	The person has medium brown skin; rarely burns.
VI	The person has deep brown-to-black skin. This person never burns.

Modified from the Skin Cancer Foundation, 2011 based on the Fitzpatrick Classification. *http://www.skincancer.org/prevention/skin-types-and-at-risk-groups.html*
Take the quiz to determine your risk factors: *http://www.skincancer.org/fitzpatrick-skin-quiz.html*

exposure to carcinogens. The scale depicted in Table 23.1 is a modified burn index showing the susceptibility of an individual to sun damage based on the person's skin type. Individuals in the type l and type II categories are at a higher risk for developing skin cancer. When coupled with other risk factors, the individual's chances of developing a skin cancer will increase. When counseling patients, it is important to determine where the individual falls on the burn index scale. The process of determining this factor also opens communication with the person.

Melanoma is the most common cancer in women aged 25 to 29 years (Skin Cancer Foundation, 2012). One blistering sunburn during childhood will greatly increase a person's chance of developing skin cancer. It is believed that the increased incidence and the increasingly young age of individuals diagnosed with melanoma have a strong correlation with tanning beds (Skin Cancer Foundation, 2012) (Box 23.1).

Malignant Skin Lesions

There are three main types of skin cancer, named for the types of skin cells from which they develop. The most deadly form of skin cancer is melanoma, and, fortunately, it is the least commonly found of the three types of skin cancer. The most commonly found skin cancers are basal cell and squamous cell carcinomas. **Basal cell carcinoma** consists of malignant nests of basal cells, is usually very slow growing, and typically does not spread. Basal cell carcinoma is commonly found on the hands, neck, and head. **Squamous cell carcinoma** is identified by malignant squamous epithelial cells. The three types of cancer are discussed in this section.

BOX 23.1 **Indoor Tanning Beds**

Young adults are especially susceptible to the damaging rays of ultraviolet light, since their cells are dividing and changing more rapidly than those of adults. In a campaign directed toward teenage girls, the American Academy of Dermatology (AAD) (October, 2006) issued a Public Service Announcement aimed at girls in the 12- to 14-year-old age group. This target population was selected because most have not started using tanning beds at this stage of life. Tanning beds emit UVA (longer wavelengths that penetrate deeply into the tissues) and UVB (shorter wavelengths causing sunburns) radiation at levels that can be as much as 15 times stronger than the sun. Annually, according to the AAD (2011), more than 28 million people tan in tanning salons in the United States. Women and girls aged 16 to 49 years make up 70% of the total number using tanning beds. Ultraviolet light is a known risk factor for melanoma, basal cell carcinoma, and squamous cell carcinoma. Research shows that indoor tanning increased a person's melanoma risk by 75%. The risk also may increase if you had breast or thyroid cancer according to the American Academy of Dermatology 2012. Currently, only 31 states regulate youth access to tanning bed facilities. However, many do not allow minors under a certain age such as 14 years old. For a list of state regulations (2012) see: *http://www.ncsl.org/issues-research/health/indoor-tanning-restrictions-for-minors.aspx.* California (2011) has become the first state in the nation to prohibit the use of indoor tanning devices for all children and adolescents under the age of 18. Other states are expected to follow in the banning of tanning salons for children. The state of California is expected to have 8,250 new cases of melanoma in 2011, placing them at 12% of the total national cases of melanoma. The rates have steadily increased for the past 30 years. Problems related to tanning beds have been compounded by the fact that the genitalia and the eyes are often not protected and are highly susceptible to the damaging radiation, since these body areas are rarely exposed to intense ultraviolet rays. Eyeglasses are usually a standard for tanning bed clients, but many individuals do not want the white areas that can occur around the eye tissue, so they remove the protective glasses while tanning. This places them for increased risk for permanent eye damage. Melanomas are known to occur on the back of the legs and the thighs. These areas are often exposed during sunbathing by teens, especially.

The bulbs in tanning beds must be monitored and replaced frequently to keep the emitted UV levels at determined standards, and some facilities have been found to fall short of this requirement, thereby causing even more exposure to the customer. The advertisements for tanning salons often purport that tanning beds are "safe" and that they do not cause skin damage. This is false, and the AAD hopes to provide the correct information to those who use tanning salons and discourage this risky behavior. (See Clinical Protocol #10 for tips on reducing the risk of skin cancer through skin protection.) Tanning salons also offer spray-on–type tans, and many offer no protection to reduce the inhalation of the spray into the lungs. This is a concern as well.

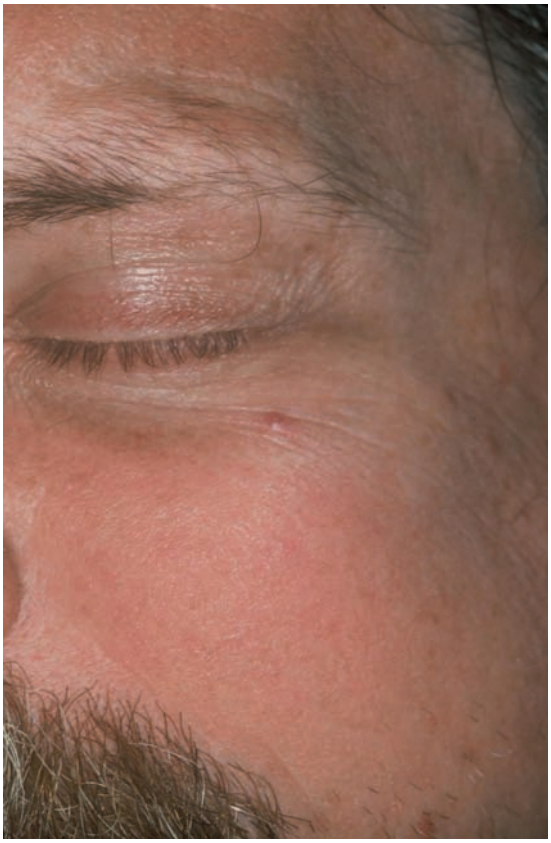

FIGURE 23.2. Basal cell carcinoma. (Courtesy of Dr. Sol Silverman, Jr.)

Basal Cell Carcinoma, Squamous Cell Carcinoma, and Melanoma

Basal cell and squamous cell carcinomas together account for most of the skin cancers diagnosed each year (see Chapter 5 for a more complete description), followed by melanoma, which accounts for 75% of skin cancer deaths according to the AAD (2012). According to the American Cancer Association (2011), both basal cell carcinoma and squamous cell carcinoma have a better than 95% cure rate if detected and treated early. Figure 23.2 depicts an early basal cell carcinoma below the left eye. Basal cell carcinoma begins as a small, elevated lesion with rolled margins and often has a pearly, iridescent-type surface.

Basal cell carcinoma is often described as a nonhealing sore; a pink growth with rolled, elevated borders; or a waxy-type lesion. As seen in Figure 23.2, basal cell carcinoma occurs often in the upper two-thirds of the face, including the eye area. The patient's glasses should always be removed to inspect the area protected by the eyeglass frame and the hairline. Metal eyeglass frames direct more heat and can often cause more damage than other eyeglass frames. A dermatologist should evaluate any changes or growths, and the patient should be referred to a board-certified dermatologist in your area. See Chapter 5 for more information on basal cell carcinoma, squamous cell carcinoma, and melanoma.

Figure 23.3 depicts a squamous cell carcinoma of the lower lip. The tissue of the lip has lost definition at the vermilion border and has obvious solar damage. Squamous cell carcinomas often have a roughened, scaly appearance and may appear ulcerated as they progress. The most vulnerable areas for these types of cancers are the sun-exposed areas of the body. The face, head, neck, hands, legs, and arms are all exposed to sun, making these areas the most affected. The lower lip is often a prime area because of the angle to the sun. The upper lip is somewhat protected. Fair-skinned individuals with blonde or red hair and/or blue, green, or gray eyes are at increased risk. However, dark-skinned individuals develop skin cancers as well and should be evaluated fully.

FIGURE 23.3. Squamous cell carcinoma. (Courtesy of Dr. John Jacoway.)

Women aged 25 to 29 (AAD, 2012) are especially affected by the most serious type of skin disease, the melanoma, because of its ability to spread quickly and to sometimes go unreported and unnoticed. Melanoma is the most common cancer in women 25 to 29 years old according to the AAD (2012). The AAD (2012) reports that one American dies of melanoma almost every hour and melanoma rates have increased for the past 30 years. The mortality rate for melanoma is highest in older white males. Melanoma may have a pigmented appearance such as brown or black mixed colors or it may be flesh-colored pink, blue, or white with irregular surfaces. The flesh tones make the lesions more difficult to see, since they blend in with the surrounding surface. Oral melanoma is discussed in Chapter 15 under pigmented lesions. Figure 23.4A shows a very early melanoma with mixed colors. Melanomas may also be found in the nail bed, mucosal tissue such as the nose, mouth, female genitals, scalp, and the eye. The flesh-tone melanoma is referred to as an amelanotic melanoma.

Melanomas are further described in the chapter on neoplasms, Chapter 5. More than 131,810 new cases of melanoma will be diagnosed in the United States this year, and 1 in 5 people will be diagnosed with skin cancer in their lifetime (AAD, 2012.) and 1 in 50 will be diagnosed with melanoma by the year 2015. In the United States, every 10 minutes someone is diagnosed with melanoma, and someone else dies of it every hour. Although melanomas affect light-skinned individuals, dark-skinned individuals may develop these on cutaneous surfaces, orally, on the soles of the feet, under nails, and on the palms of the hands. Melanoma is 10 times more common in whites than in blacks.

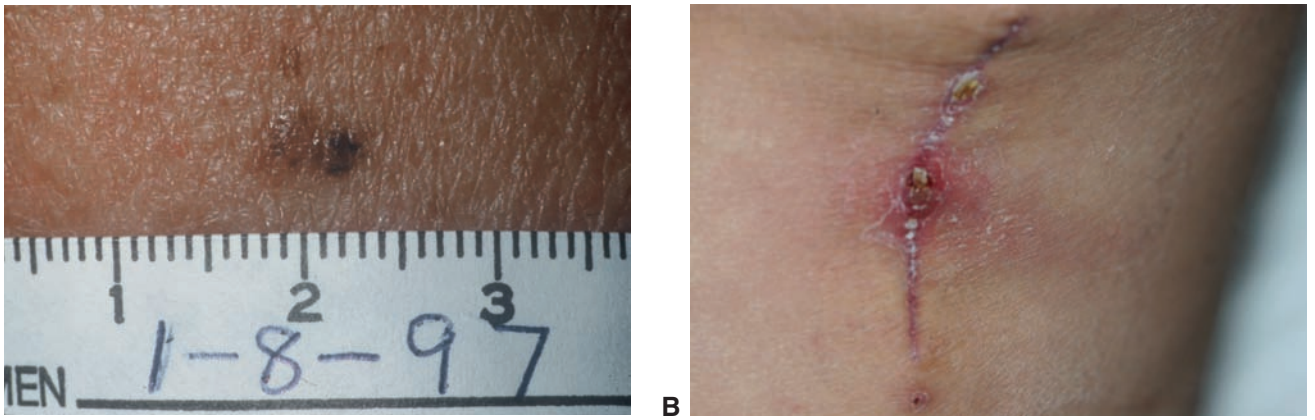

FIGURE 23.4. **A**. Melanoma. (Courtesy of Dr. Michael Brennan.) **B**. Postsurgery scar after removal of a melanoma from patient's leg.

Because of the large amount of surrounding tissue that is removed to obtain clear margins, surgery is often extensive for even moderate-size melanomas. Figure 23.4B shows the scar that remained postsurgery for the removal of a melanoma on the upper leg of a 23-year-old female. This patient had at least four visits to tanning beds in the two years prior to developing the melanoma. The melanoma removed was 3 mm in diameter, but as seen in the figure, the amount of tissue that needed to be removed to get clear margins was extensive. The incision line reached 4 inches, and the initial melanoma measured 3 mm. Finding the melanoma in its earliest stages means a high cure rate, less-invasive surgery, and possibly avoidance of chemotherapy/radiation in some cases.

Skin changes are evaluated by what is termed the "ABCDEs" of skin cancer (for more details, see "Neoplasia," Chapter 5). Essentially, any changes in the following criteria should be noted and referred to a dermatologist for further evaluation:

A. Asymmetry: A lack of uniformity in both sides of the suspected lesion
B. Border irregularity: Edges of the lesion may be blurred, notched, or ragged
C. Color variation: Lesion may show shades of tan, brown, or black with red pigments, or possibly white, blue, or black
D. Diameter: Noted with concern when the lesion is more than 6 mm, or larger than a pencil eraser
E. Evolving: Any new or changing growth should be evaluated.

If a patient has any of the above-mentioned ABCDEs, the practitioner should suspect the possibility of cancer. Digital photography is an excellent tool for capturing the status and documenting future changes. The images can be stored and used for comparison in future visits. This type of photography is easily transferred to another practice if the patient changes geographic locations. In addition, mole-mapping procedures are available that measure, record, and store data for future comparison. See the Media Menu at the end of this chapter for information on the ADA Mole Map.

Although basal cell carcinoma, squamous cell carcinoma, and melanoma are the most commonly seen skin lesions, other types of skin lesions may require some investigative approaches to determine their classification. We present

APPLICATION 23.1

The extraoral screening for skin lesions and external signs of disease are important in early cancer and disease prevention, recognition, and treatment. Making your office known for such screening promotes the office and reflects the importance your office places on both intra- and extraoral cancer screening. This could be done with a button logo worn by the office personnel, which also serves as a good way to have all the office members, including assistants, office managers, and receptionists, vested in a common goal. The Oral Cancer Foundation *(http://www.oralcancer.org)* offers such buttons. Your office could design your own or perhaps order a type that has been designed by the Oral Cancer Foundation such as "I Save Lives." The logo that is chosen could even be displayed on letterhead, Web sites, and perhaps the bags that are used for dental products given to the patient (Fig. 23.5).

FIGURE 23.5. Examples of oral cancer screening buttons.

APPLICATION 23.2

Your receptionist has just returned to work this afternoon with a great tan. She has in her hand some brochures with free coupons from the tanning salon two blocks away. Her intent is to distribute these to patients and to leave them in the waiting area. Your practice is a family practice, and many of your patients are 10 to 20 years of age.

What would you say to the receptionist regarding tanning beds?

- What would you tell the receptionist about tanning beds and about skin cancer that may help to justify why she cannot place such brochures in the office? Refer to information within the chapter.
- Use Figure 23.4B to demonstrate the extent of the damage caused by a melanoma. Remember that the patient used a tanning bed only several times.

some other common types of skin lesions in this chapter because the possibility is real that hygienists will see them at some point in their clinical practice.

Premalignant Skin Lesions

Actinic Keratosis

Actinic keratosis also called solar keratosis, is the most common type of precancerous skin lesion. Actinic keratoses are scaly or crusty patches appearing on the skin surface. The most common locations are the backs of the hands, the cheek, ear, forehead, and lower lip. It is necessary to remove the glasses of a patient so that the areas under the frames can be thoroughly evaluated for any lesions. The eyeglasses may be even more detrimental to the skin when they are metal, since they may intensify the reflection of the sun to the skin in that area. Living in a geographic location closer to the equator plays a role in the development of some skin lesions; however, even people in the colder climates may develop actinic keratosis as well as other types of skin lesions. For example, sunburned snow ski instructors may be prone to developing skin lesions because of the amount of time that they spend in the sun. The snow also reflects the sun and intensifies the exposure even more.

Classically, the lesions associated with actinic keratosis appear to be dry and rough textured but usually do not have erosion as a typical characteristic. Figure 23.6 shows a patient with an early actinic keratosis skin lesion. Clinicians must pay attention to these lesions because they may be the first step in the development of squamous cell carcinoma. The lesions occur because of long-term exposure to the sun. Often, the lesions develop slowly and may wane, only to reappear later. Individuals who have multiple areas of actinic keratosis have had substantial exposure to the sun, increasing their risk of developing all types of skin cancer. The usual treatment for actinic keratosis removal is cryosurgery, curettage and desiccation, laser surgery, photodynamic therapy, and topical medications. (See Clinical Protocol #10 for sun protection guidelines.)

FIGURE 23.6. Actinic keratosis.

Actinic Cheilitis

Actinic cheilitis, or solar cheilosis, is a form of actinic keratosis that develops on the lips and may evolve into a type of squamous cell carcinoma that can spread rapidly to other parts of the body. Sun damage manifests clinically as fairly distinct stages of tissue destruction. The lips may appear scaly and crusted, with a loss of definition of the vermilion border of the lip (Fig. 23.7). The dental practitioner should recommend further evaluation, referral to a dermatologist, and the use of a lip balm with sunscreen. All patients should be advised to use lip balm or lipstick with sunscreen, having an SPF of at least 15. Lip balms that block the UVB/UVA rays are the most effective in protecting the lip area. The lower lip may appear wrinkled, uneven, with loss of the vermilion border, and pigmented with multiple areas of discoloration, depending upon the level of destruction. As with other sun damage to the skin, the most vulnerable patients are those with fair-to-light skin. Smoking increases the risk of many cancers but also increases the risk of actinic cheilitis because of the direct exposure of this area to chemicals and heat.

Benign Skin Lesions

Acrochordon

Acrochordons are skin tags that may be somewhat stalk-like or pedunculated. Skin tags are usually small, slender stalks of tissue that are typically flesh colored and blend in with the surrounding tissue (Fig. 23.8). These tags are benign and pose no problem for the patient but should be noted in case of any future changes. Some reports have suggested an association with the acrochordon and colon

FIGURE 23.7. Actinic cheilitis.

polyps as well as diabetes (Bhargava et al., 1996). Other studies have found no association with colon polyps and skin tags (Akhtar and Zhuo, 2003) in a minority population.

Comedones

Comedones are dilated hair follicles that are filled with keratin, bacteria, and sebum. In the case of open comedones, the lesions become trapped with a blackened mass of epithelial debris. Comedones are mentioned in this discussion to differentiate them from nevi. The patient usually has a history of exposure to the sun and harsh elements. Comedones stem from solar damage and solar elastosis.

FIGURE 23.8. Acrochordon. (From Goodheart HP. Goodheart's photoguide of common skin disorders. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

Favre-Racouchot disease is a common disease characterized by solar elastosis and large open comedones and cysts in varying sizes. The disorder typically affects white men who spend a lot of time in the sun with excessive exposure to UV light. Smoking is strongly associated with this as well. The comedones may appear similar to those in acne without the inflammation that would usually occur with dermatologic problems. The orbital, temporal, and lateral canthi are prime locations for comedo. Tretinoin (vitamin A acid, retinoic acid) is used in the treatment because the expulsive action of the topical medication decreases comedone formation. Referral to a dermatologist is recommended.

Figure 23.9 depicts blackened comedones in multiple areas around the lower area of the eye.

Eczema

Eczema is a general term for an inflammatory response of the skin to multiple agents and is often associated with hypersensitivity type 1 reactions. In Figure 23.10A, the patient has a contact eczema hypersensitivity response, as well as an inflammatory skin response (Fig. 23.10B). Occupational contact eczemas are commonly found in individuals who wash their hands frequently such as dental, medical, and laboratory workers. Additionally, individuals who have exposure to certain chemicals and multiple types of agents may exhibit eczema. In this particular case, the patient was reacting to the cherry flavoring agent in a lip balm. There are two forms of ectopic eczema: infantile and adult. The infantile type may exhibit more obvious ulcerative-type lesions and usually has some causative agent. An example

FIGURE 23.9. Comedones.

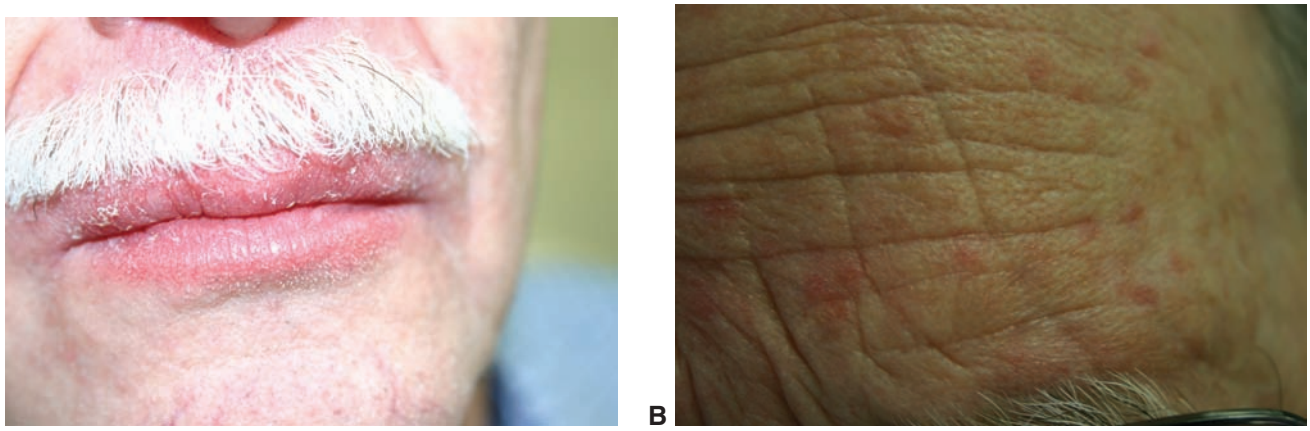

FIGURE 23.10. **A**. Eczema on lips. **B**. Allergic response on forehead.

would be rashes caused by diapers, skin medications, or candidiasis infections. Usual symptoms include dryness, pruritus, and inflammation. Topical steroids are prescribed in severe cases; however, most cases dissipate on their own.

Ephelides (Freckles)

Freckles are usually found in sun-exposed areas of skin. **Ephelides** are flat, pigmented macules less than 0.5 cm that exhibit increased melanin when viewed microscopically. Freckles tend to be found more commonly on people who have light complexions, and the ephelides become more intense with sun exposure. Most tend to be more prevalent in children and fade in adulthood.

Keloid

Keloids are hyperplastic scar tissue and are more common in blacks. Keloids are covered in Chapter 3. Figure 23.11 depicts a black woman with a keloid on the forehead and on the nose.

Solar Lentigo

Solar lentigo spots are benign macules caused by sun exposure. They are usually larger than freckles and fade more easily when sun exposure is diminished. Figure 23.12 depicts a lentigo spot on the arm of a patient. When they occur periorally, disorders such as Addison disease (Chapter 7), Laugier-Hunziker (Chapter 15), and Peutz-Jeghers syndrome (Chapter 10) may be considered. These spots are sometimes called liver spots or age spots and are notoriously found on the backs of the hand as individuals age. Lentigos are benign and vary in number with the individual and the amount of cumulative sun exposure.

Milia

Milia (plural of milium) are small subepidermal keratinous cysts (also called epidermal inclusion cysts) that develop usually on the eyelid or facial surfaces. They may be removed for cosmetic reasons or may sometimes dissolve on their own, since they are close to the skin surface. Often, the cysts will be expelled during normal face washing. Figure 23.13 shows small white milia found on the patient's forehead.

Nevi

Acquired melanocytic **nevi** (plural; singular, *nevus*), commonly called *moles*, may be visible on the face, neck region,

FIGURE 23.11. Keloid. (Courtesy of Dr. Carolyn Bentley.)

FIGURE 23.12. Solar lentigo.

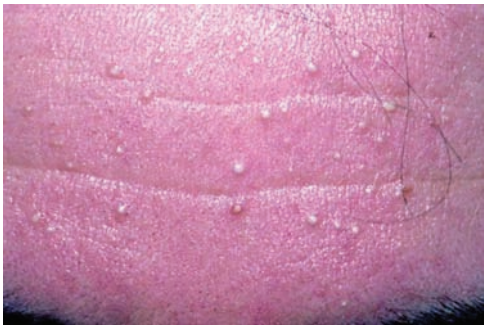

FIGURE 23.13. Milia. (From Goodheart HP, MD. Goodheart's photoguide of common skin disorders. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

and virtually any part of the skin seen by the practitioner. Figure 23.14 is a classic nevus on the neck. A mole is a collection of nevus cells in the dermis or the epithelium, with a variation of types of nevi. The nevi are classified into junctional and compound types. Nevi usually have a smooth surface, sometimes pebbled, and may be flesh colored or pigmented, ranging in size from 0.1 to 0.6 mm. Moles usually begin in childhood and may increase in adulthood, with removal when there is an abnormal appearance or some questionable characteristic. More than 50 moles may be associated with an increased risk of skin cancer. Sometimes changes can be subtle, and extraoral photography and mole mapping (digitally documenting all moles) are very important.

Perlèche (Angular Cheilitis or Angular Stomatitis)

Perlèche occurs at the commissures of the mouth, and these skin lesions may appear red and crusted and sometimes as open wounds. Also called **angular stomatitis**, perlèche lesions are caused by *Candida*, loss of dimension due to aging, and may be involved in vitamin B deficiencies in older populations as well. The lesions result from saliva infected with *Candida* resting in the folds of skin at the commissures. Figure 23.15 depicts *Candida* at the commissures with an erythematous area visible. Perlèche is commonly found in the elderly and especially edentulous patients.

FIGURE 23.15. Perlèche. (Courtesy of Dr. Terry Rees.)

Pityriasis Rosea

Pityriasis is an inflammatory dermatosis of unknown etiology. Some studies suggest that an infective agent may be responsible, but no conclusive evidence exists to support any viral or bacterial agent. The condition is self-limiting, pruritic, and reported most commonly in the spring and fall. Most affected are individuals between the ages of 10 and 29 (Chuh et al., 2005). The lesions are typically red to pink, with oval or round shapes, and average from 2 to 10 cm. The center part of the lesion has been described as a deeper salmon color. Figure 23.16 shows an oval pityriasis lesion on a patient's back exhibiting a darker external halo.

Poison Oak

Poison oak causes a skin reaction after exposure, producing multiple vesicle-like lesions. Poison oak belongs to the species of plant called the *Toxicodendron* family, which includes poison oak, poison sumac, and poison ivy. Contact with poison oak, poison ivy, or poison sumac often produces an allergic reaction such as the one seen in Figure 23.17.

FIGURE 23.14. Nevus.

FIGURE 23.16. Pityriasis.

FIGURE 23.17. Poison oak.

Psoriasis

Psoriasis affects approximately 7.5 million people in the US population (AAD, 2011) and usually occurs in younger adults between 15 and 30 years of age; 80% of those affected have the plaque form of psoriasis. Other forms of psoriasis affect an older population, occurring in the 50- to 60-year-old age range. The dental hygienist can expect to see the skin disorder at some point clinically. Psoriasis has a classic appearance of red, plaque-like lesions covered with a white, thin scale that has a pearly, iridescent characteristic surrounding the lesions. The condition may have many different forms but commonly exhibits a scaly, pearl-like appearance. Removal of the scales may produce bleeding. Figure 23.18 depicts an area behind the ear that exhibits scaling. Psoriasis is often episodic, with periods of exacerbation (increased severity) and quiescence (inactive state). Pruritus (itching) is a common complaint. Several factors appear to be involved in the occurrence of psoriasis: a genetic predisposition, environmental factors, and certain stimuli such as trauma, infections, and sun exposure/cold exposure. Many people report that they developed the condition after a medication such as lithium or medicine to prevent malaria. Stress, a bout with strep throat, a cut, a scratch, and cold, dry weather are implicated as well. It is not contagious. Treatment varies and includes the use of corticosteroids, coal tar products, and other topical agents. Sometimes light therapy is used.

FIGURE 23.18. Psoriasis. (From Goodheart HP. Goodheart's photoguide of common skin disorders. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

FIGURE 23.19. Rhinophyma. (From Goodheart HP. Goodheart's photoguide of common skin disorders. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2003.)

Rhinophyma

Rhinophyma is seen on the nose, and the sebaceous glands are enlarged appearing swollen, with increased fibrosis and vascularity. Seen more in males and often called "hammer nose," the enlarged glands are referred to as rhinophyma. **Telangiectasia**, or enlarged capillaries, may also be present, with obvious dilated capillaries visible. Figure 23.19 depicts the enlarged glands of the nose on a male patient. Rhinophyma is an extension of rosacea/acne. The prime physical problem resulting from the disorder is blockage of the nose and a limited ability to breathe when severe. The triggers associated with rhinophyma are sun, stress, and climate changes such as hot, cold, and humidity.

Rosacea

Rosacea is typically seen on the nose and cheek areas and exhibits redness with chronic vascular and follicular dilation. Figure 23.20 depicts a cheek area that exhibits rosacea with a reddened skin area. The sebaceous glands may be hyperplastic, and the pustules may be erythematous. Rosacea is characteristic of some systemic diseases, such as lupus, which exhibits the chronic butterfly rash in the malar area.

FIGURE 23.20. Rosacea.

FIGURE 23.21. Seborrheic keratoses.

Seborrheic Keratoses

Seborrheic keratoses will vary from light brown to black and may appear as multiple or singular lesions. The lesions often appear in middle age and increase as the person ages. Because of the corrugated appearance of the growths, they may be confused with warts. Seborrheic keratosis is characterized by the overproduction of sebum by the sebaceous glands, causing overproduction of the horny layer of the skin. Unlike actinic keratoses, it is benign and not precancerous.

Figure 23.21 depicts the hairline of a patient who has an area of raised, pigmented seborrheic keratosis. The lesions usually do not require treatment, but they may be removed with cryotherapy or curettage and electrodesiccation. Once removed, they do not usually return. Any lesion can cause irritation from scratching, injury, etc., so they are often removed for cosmetic reasons.

Urticaria

Urticaria is also known as hives or allergic reactions and is covered thoroughly in Chapter 4. The clinician may notice hives in a patient who is reacting to a substance, insect, medication, the sun (sometimes called sun poisoning), excitement, or possibly a systemic disease. A wheal is a plaque or papule produced because of edema within the skin. The wheals may be slightly reddened and may be coalescing or single. Figure 23.22 depicts skin reactions to certain metals such as zinc, gold, nickel, chromium, and silver. The lesions are due to a histamine reaction evoked during allergy testing. The treatment is often antihistamines, corticosteroids, epinephrine, and identification of the offending substance.

Xanthelasma

In xanthelasma, the lower eyelids often exhibit a pale yellow-orange raised area that is usually in the corner of the eye (Fig. 23.23). The plaques are benign and are only removed for cosmetic reasons when there is a large noticeable discoloration. On examination, the lesion may appear as a cyst or other skin lesion. The lesions are predominately lipid material, are benign, and pose no problem to the patient. The papules have been associated with hyperlipidemia and with low-density lipoproteins. The patient should be advised to have his or her cholesterol levels checked. High levels may need medications and/or lifestyle changes to decrease the cholesterol levels.

FIGURE 23.22. Urticaria. (Courtesy of Dr. Peter Jacobsen.)

Diseases Associated with Skin Lesions

Certain disorders may also have oral skin lesions as part of the infection or disease. The diseases listed below have cutaneous manifestations, and the skin component may often be seen before any other systemic reactions. The dental hygienist may notice a lesion and question the patient before he or she is even aware that a systemic infection is occurring.

Erythema Multiforme

Erythema multiforme is caused by drug sensitivity or possibly by exposure to any of the following: herpes simplex

FIGURE 23.23. Xanthelasma.

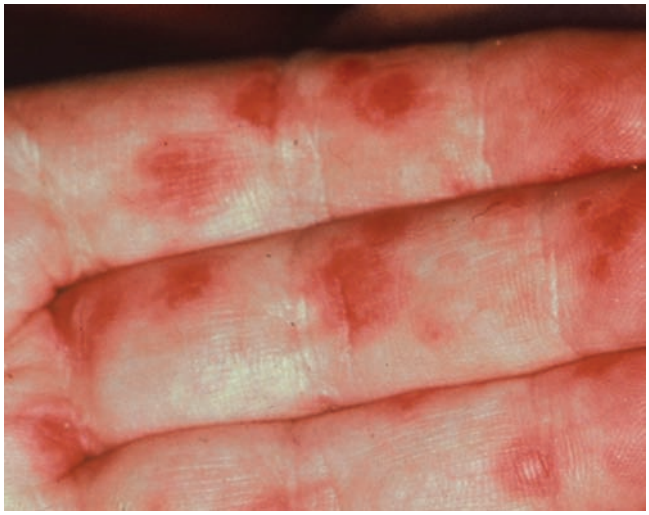

FIGURE 23.24. Erythema multiforme. (Courtesy of Dr. Peter Jacobsen.)

infection, mycoplasma, tuberculosis, or histoplasmosis. In severe cases, the patient may be treated with systemic corticosteroids. The severe form (discussed in Chapter 12) is termed Steven-Johnson syndrome. Most often, the lesions subside within a few weeks. Oral lesions are reported in up to 50% of cases (Regezi et al., 2003). Erythema multiforme is covered in Chapter 12. Figure 23.24 depicts the fingers of a patient with the classic target or iris lesions.

Graft versus Host Disease

Graft versus host disease (GVHD) primarily occurs in association with bone marrow transplants, although it may occasionally follow solid organ transplantation. Essentially, the grafted bone marrow recognizes the tissues of the host as foreign and attacks them. GVHD occurs in up to 45% of bone marrow patients, and the oral cavity may be involved 80% of the time (Imanguli et al., 2006). It can occur as an acute reaction within days of the engraftment or as a chronic condition months to years later. GVHD may affect the liver and other organs, but skin and oral mucosa are often involved as well. Figure 23.25A depicts the arm area of a black man with GVHD exhibiting a loss of pigmentation in areas of the skin, causing a spotted appearance. Figure 23.25B shows the facial area of the same patient, exhibiting a loss of pigmentation on the face and the lips, causing a diffuse, spotted appearance. Skin lesions may be similar to those found in lupus erythematosus, scleroderma, or lichen planus. Loss of pigmentation (vitiligo) is a relatively common skin manifestation of chronic GVHD. Oral manifestations include lesions similar to lichen planus, lupus erythematosus, or nonspecific mucosal ulcerations.

Impetigo

Impetigo is highly contagious and is caused by infection with *Staphylococcus aureus* and streptococci organisms. Nonbullous impetigo is the most common pediatric skin infection and usually starts in a traumatized area. The lesion usually begins as an erythematous papule that becomes pustular and ruptures with a yellow, crusted appearance. The lesions may also be in a bullous form that accounts for only about 30% of cases (Edlich et al., 2005). Figure 23.26 shows typical lesions related to impetigo around the nose and mouth of a child. Impetigo is predominately seen in children and groups that are in close proximity, such as children in day care centers. Topical and systemic antibiotics are necessary. Dental treatment should be postponed because of the highly contagious nature of the disorder and the fact that it will spread to other parts of the face and body of the patient.

Lichen Planus

Lichen planus is both an oral and cutaneous disorder that produces a variation of mucosal disturbances such as ulceration, plaques, erosion, and skin lesions. The red and white forms of oral lichen planus are discussed in Chapters 13 and 14, respectively. In this chapter, we mention the skin lesions related to lichen planus that a practitioner may discover during a routine examination. Although lichen planus is most often noted intraorally, some patients may have external lesions as well. Approximately 5 to 45% of those with lichen planus have both oral and cutaneous lesions at some point in time (Plemons et al., 1999). Additionally, other

A **B**

FIGURE 23.25. **A** and **B**. Graft versus host disease (GVHD).

FIGURE 23.26. Impetigo. (From Goodheart HP. Goodheart's photoguide of common skin disorders. 2nd ed.. Philadelphia: Lippincott Williams & Wilkins, 2003.)

mucosal diseases such as pemphigus and pemphigoid may exhibit skin lesions. These types of skin lesions have a different appearance from that of lichen planus in most cases but can appear similar in some instances. Some skin lesions may be so subtle that they are often not noticed or recorded as lichen planus. When lichen planus appears on the skin, the lesions appear as keratotic, purple, pruritic plaques that occur most frequently on flexor surfaces as seen in Figure 23.27A, depicting a female with lichen planus on the lips, and Figure 23.27B, showing lichen planus lesions on the arms with pink to purple raised plaques.

Lupus

Lupus erythematosus is an autoimmune disease described as an inflammatory connective tissue disease. Lupus is covered in more detail in Chapter 12. Skin lesions related to systemic and discoid lupus may be recognized as having the classic "butterfly rash" that is often found across the nose and malar processes. The skin involvement may be in the scalp region as in Figure 23.28A, which shows a patient with systemic lupus erythematosus who has scalp lesions and wears a wig to cover the area. In Figure 23.28B, the patient exhibits cutaneous lesions below the right eye. Sometimes oral tissues may be affected as well. Systemic lupus erythematosus is very serious and may affect vital organs.

Sarcoidosis

Sarcoidosis is a granulomatous disease of unknown cause that often affects blacks but may occur in any ethnic group. Currently, a mycobacteria or Epstein-Barr virus has been suggested. Sarcoidosis is a systemic disease affecting multiple organs, skin, eyes, and especially targeting the lungs, exhibiting interstitial fibrosis. The disease causes the formation of granulomas composed of epithelioid and multinucleated giant cells. Cutaneous lesions occur in about 25% of cases (Fatahzadeh and Rinaggio, 2006), with skin and eye lesions apparent. Figure 23.29 shows a male with facial skin involvement exhibiting pronounced, raised lesions on the nose and around the lip area. Enlargement of the salivary glands is often the first characteristic that is noticed in the development of sarcoidosis, and xerostomia is commonly reported by patients. (Sarcoidosis is covered in Chapter 17.)

Scleroderma

The term progressive systemic sclerosis is synonymous with systemic **scleroderma**. Scleroderma has an unknown etiology but is classified as an immune dysfunction disease. Normally affecting women (4:1) and usually occurring in middle age, scleroderma may occur in children as well (Laxer and Zulian, 2006). The disease may occur in two forms: a generalized progressive systemic form and a diffuse cutaneous form termed morphea. Both forms manifest with progressive thickening and tightening of the skin in all areas. The lungs, skin, gastrointestinal tract, musculoskeletal system, heart, and kidney are affected by fibrosis and extensive collagen production. En coup de sabre (cut of the sabre) is a localized thickened area of skin, appearing as a knife wound. This is sometimes found in this disorder within the gingiva. Typically, the disease occurs in conjunction with rheumatoid arthritis, lupus erythematosus, dermatomyositis, and/or Sjögren syndrome. **Raynaud**

A

B

FIGURE 23.27. **A**. Lichen planus. (Courtesy of Dr. Summer Shapiro.) **B**. Lichen planus. (Courtesy of Dr. Terry Rees.)

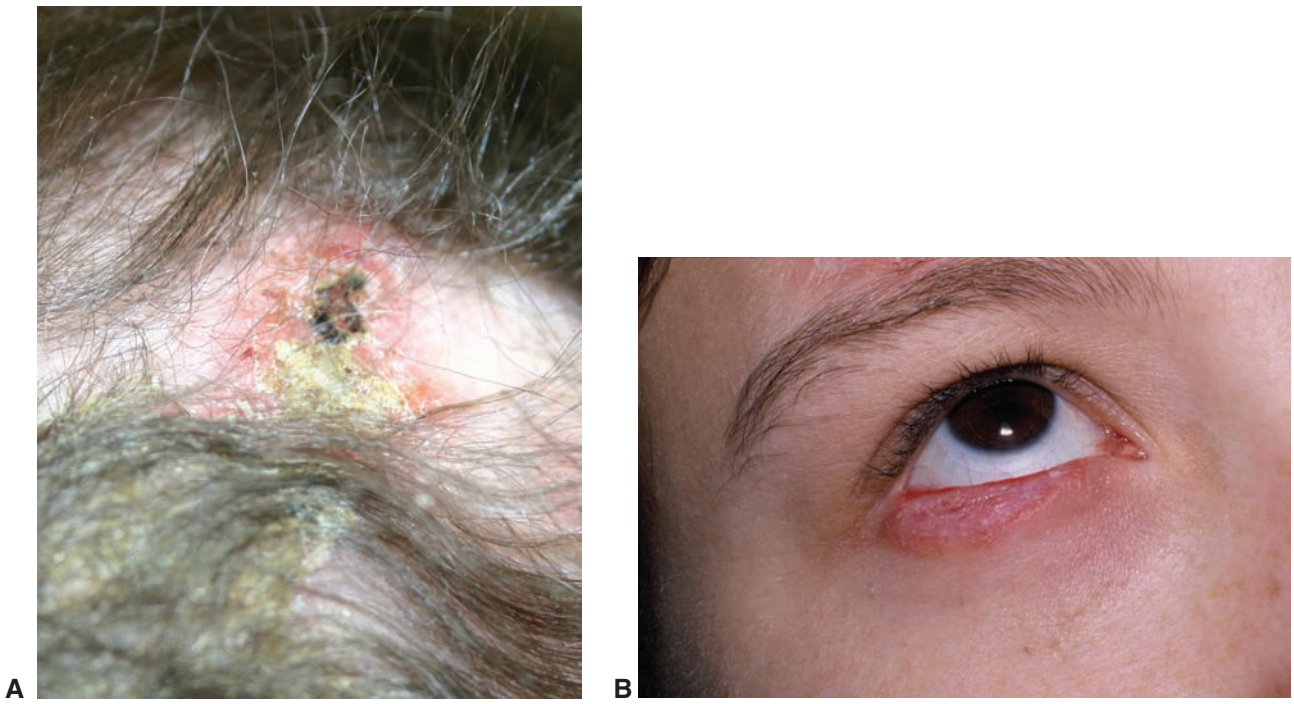

FIGURE 23.28. **A**, **B**. Lupus.

phenomenon is found in conjunction with the above-mentioned diseases and is characterized by numbness and pallor of the fingers, toes, and nose due to intermittent lack of blood flow. Major organs are affected with fibrosis, and the skin is usually first noticed. The skin becomes less mobile, exhibits rigidity, and becomes tightly elastic. The thickening or hardening of the skin is termed **sclerodactyly**. The fingers become shortened and stiff and exhibit fibrosis. The localized type of scleroderma is known as morphea. Figure 23.30 shows the hands of a patient with sclerodactyly, with fingers in a rigid posture with Raynaud phenomenon depicted as well.

The oral structures become rigid and cause the perioral tissues to become constricted, thereby limiting the opening of the mouth and esophagus (Gold et al., 2007; Leader, 2007). This can cause the patient major difficulty with oral hygiene and eating. The disease can also cause resorption of the facial bones and fibrosis of the salivary glands, leading to xerostomia and contributing to an increase in caries. Periodontal ligament widening and idiopathic resorption of teeth and bone may occur. Telangiectasia increases the risk

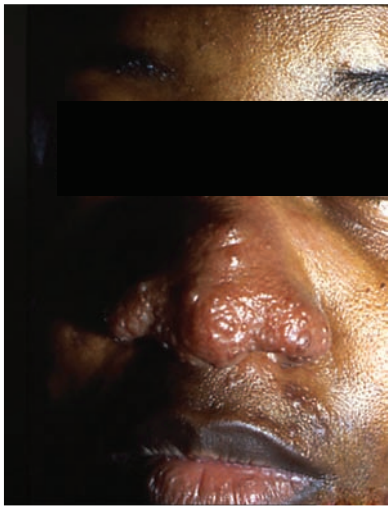

FIGURE 23.29. Sarcoidosis. (Courtesy of Dr. T.D. Rees.)

FIGURE 23.30. Sclerodactyly. (Image provided by Stedman's.)

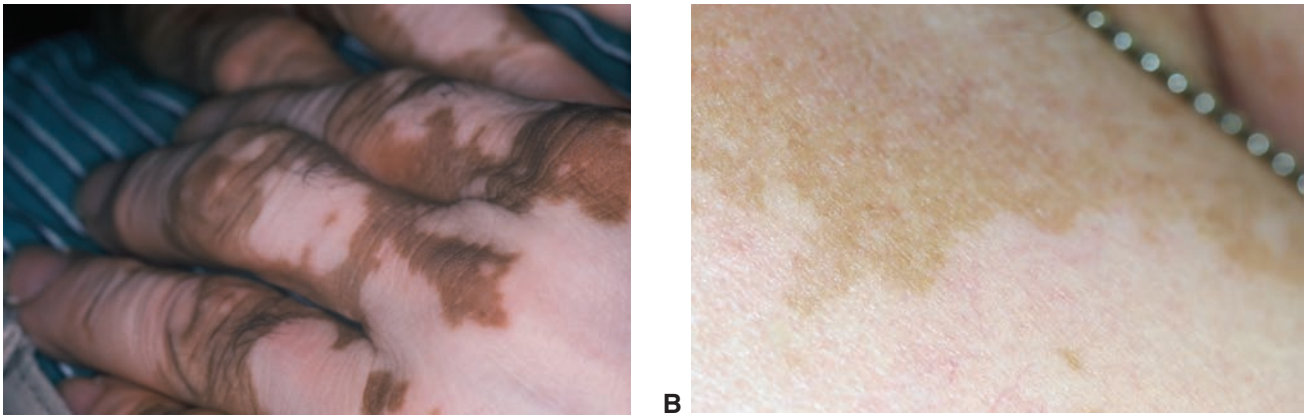

FIGURE 23.31. **A**, **B**. Vitiligo.

of spontaneous internal bleeding and fibrosis of the esophagus, causing difficulty in swallowing with eventual destruction of the esophageal wall. **CREST syndrome**, which is characterized by calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia, is associated with systemic scleroderma.

Vitiligo

Vitiligo is an autoimmune disorder that is characterized by a lighter appearance of the tissue due to loss of pigment and destruction of melanocytes. The disorder involves 1% of the world population (Whitton et al., 2006; National Vitiligo Foundation, 2011), and approximately 2 to 4 million individuals in the United States alone, with varying degrees of melanocyte destruction. The cause of the disease is unknown, but exposure to chemical substances is suspected, with the largest class of chemicals being phenolic/catecholic derivatives. Other causes that have been suggested are deficiency in an unidentified melanocyte growth factor, alterations in the mechanisms of the melanocyte, and breakdown in free radical defense in the dermis. Figure 23.31A shows vitiligo with loss of pigmentation on the hands of a black male patient. Figure 23.31B shows the back and shoulder area of a white female with vitiligo. The contrast of the loss of pigmentation is, of course, not as great in the white woman. The disease occurs in both males and females, usually beginning in the second decade of life.

Warts

Warts are a common name for verrucae vulgaris and may also be referred to as plantar warts or flat warts (see Chapter 16). These lesions are benign and caused by various strains of the human papillomaviruses (HPV). Warts appear as papillary lesions and are usually difficult to remove because of their ability to spread. When found on the fingers, the virus is sometimes transferred to other areas of the body such as the face, lips, nose, and genitalia. Over 70 types have been identified. Cervical cancer related to HPV is the most significant factor in women. Most external lesions regress spontaneously, but some may need other means such as surgical excision, cryosurgery, or application of certain acids.

Leishmaniasis

Leishmaniasis is a disease that is found primarily in tropical and warm climates throughout the world. The southern United States is also an area where we are discovering leishmaniasis. Cutaneous leishmaniasis can be found in at least 88 countries and affects as many as 12 million people worldwide, with 1.5 to 2 million cases a year (Paz et al., 2011). Leishmaniasis is caused by a parasite belonging to the genus *Leishmania*, and it is transmitted by the bite of female sand flies. There have been over 20 types of various types of *Leishmania* species identified, and they are found in different geographic locations of the world. Cutaneous leishmaniasis is often found in animals that have been infected by the sand fly. Outbreaks occur when animals, sand flies, and humans coexist. Cutaneous leishmaniasis is epidemic in the tropics and neotropics (Reithinger et al., 2007). The disease may be widespread, affecting multiple areas and resulting in small nodules to large mucosal tissue destruction. Smear samples are often taken to confirm the parasite depending upon the capability of the geographic area and the availability of labs with microscopes. The disease usually dissipates with time but may cause major tissue destruction before resolution.

Generally, after the person is bitten, the area of contact develops a small papule and then a nodule continues to progress and enlarge into the deeper tissues (Figure 23.32). This may continue from 2 to 6 months. The person may become immune to that species after healing, imparting lifelong immunity to the person. Lymph nodes may be enlarged and the scar that is incurred may be extensive and lifelong. Reithinger et al. (2007) state that susceptibility to cutaneous leishmaniasis is influenced by malnutrition, immunosuppression such as HIV status, and host genetic susceptibility. A differential diagnosis would include skin cancer, tuberculosis, leprosy, and possibly other skin diseases. The World Health Organization recommends treating cutaneous leishmaniasis with pentavalent antimonial drugs but most cases will resolve on their own. The scar that

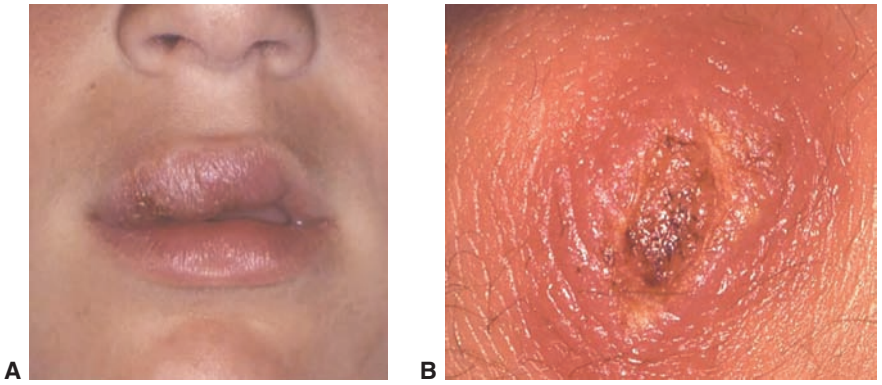

FIGURE 23.32. Cutaneous leishmaniasis. **A.** Lip lesion. **B.** Lesion on the arm of patient. (Image provided by Doron J. Aframian, DMD, PhD.)

is left especially on the facial area is of prime concern. The patient is left with less scarring when treatment is started early in the disease process. The length and the extent of treatment will vary with the geographic location and its capabilities. The type of species that caused the infection affects the type of medications that are used. Prevention and control of the sand fly continue to be a major problem in parts of the world. With many United States citizens currently in the zones of war areas where sand flies are found, it is very likely that the hygienist will encounter this entity with returning military. Many world travelers are also at risk and may not be easily diagnosed after returning to the United States.

SUMMARY

The dental office is in a unique position for both detecting and monitoring premalignant and malignant skin lesions. As discussed throughout the chapters, many diseases have oral manifestations before any other sign of disease is present. An added benefit of screenings in the dental practice is that we may be the only practitioners that the patient visits twice a year. Routine dental visits have increased in the past decades, and the dental hygienist and dentist may be the key health care providers who treat the patient most frequently. The increased dental visits may be due to social factors or pressures related to the public awareness and the wish to have a nice smile and a healthy mouth. We should be aware that we could be the only persons who may screen and evaluate the patient for skin cancer as well. If dental offices make this routine, many early cancers and disease states can be detected, and the patients may be referred to a dermatologist or other health care provider for treatment early before the disease progresses. External clues to diseases are often evident as well and the extra oral examination of the patient is important in assessing the total patient.

Signs of Skin Cancer

- Asymmetry
- Border irregularity
- Color varied
- Diameter greater than 6 mm
- A noted change in any skin lesion
- A mole or lesion that does not heal
- Bleeding within or around a mole or any growth

CHAPTER REVIEW

Case Study 23.1

The image depicted in Figure 23.33 is a skin cancer. The patient is a 45-year-old male. He noticed the area on the right side of his nose some time ago but works on a fishing boat and has not found the time to have the area checked by a dermatologist. He is a smoker and also consumes alcohol on a regular basis. He reports that he does not use any type of lotions or creams, including SPF protection.

1. What evidence can you document about this patient that would suggest that this is a skin cancer?
2. Describe what you see in this image. What type of skin cancer do you think this might be?
3. What questions would you want to ask any patient with obvious sun damage or the patient who has potential for high-risk sun damage?
4. What known risk factors would you be concerned about with regard to this particular patient?
5. What suggestions would you make regarding the lesion and future protection of the skin to all patients?
6. Do you believe that his outcome would be favorable?

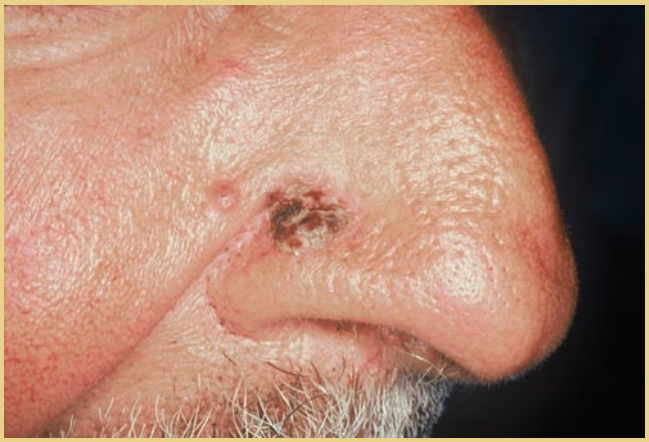

FIGURE 23.33. (Courtesy of Dr. Sol Silverman, Jr.)

For answers and additional review activities, log in to **thePoint.lww.com**

Case Study 23.2

Your patient is a 26-year-old female who is a nonsmoker with no known health conditions. She does not eat a healthy diet on most days but does some exercise. The lesion that is on her lower thigh (Fig. 23.34) has been present and noticed by the patient for the past 6 months. It causes no pain, but she does not like the appearance.

1. Using the ABCDE criteria for assessing skin lesions, describe the growth depicted in the image.
2. What would you expect is occurring beneath this growth microscopically?
3. How serious do you think this lesion is? List your differential diagnosis.
4. What would you recommend to this patient?

FIGURE 23.34. (Courtesy of Dr. Sol Silverman, Jr.)

For answers and additional review activities, log in to **thePoint.lww.com**

Critical Thinking Activity

Study Figure 23.25 and note the appearance of the patient's lips. Sun damage is apparent in this patient because of the following:

- There is a loss of definition of the vermillion border on the lower lip.
- The tissue is crusted, not smooth surfaced as would be seen in healthy tissue.

Respond to the following:

1. Do you think the patient has sun damage? If so, why? What are you noting that would be characteristic?
2. What can you tell by her appearance in the figure?
3. What would you do before you started any type of dental procedure?

FIGURE 23.35. (Courtesy of Dr. Sol Silverman, Jr.)

4. Do you think the patient would be uncomfortable or suffer any pain from the lips?
5. Do you think she would have any emotional conflict with her appearance?
6. Are there any specific diseases that you would want to ask about when you take her medical history?
7. What do you think are the possibilities regarding an etiology?
8. What questions would you ask the patient?
   - **A.** What is the sun exposure history?
   - **B.** Does she use a sunscreen and a lip balm with a sunscreen of at least SPF15 or higher?
   - **C.** How long has it been since she changed her lipstick? (This may be a factor in an allergic-type response to a cosmetic or a dental product. New products should be evaluated.)
   - **D.** Does she bite or lick her lips constantly? (During the conversation, evaluate whether she is actually biting, chewing, or licking her lips, since some patients may not even be aware of the habit.)

NOTE: Vaseline on the lips would be relevant to any dental treatment since the patient's lips are dry and crusted. Any manipulation will cause them to bleed. Vaseline is not the best choice for daily care and treatment of the lips. Simple lip balms with few additives and few petroleum products are best tolerated. Flavoring agents may cause problems for some individuals. Most patients do well when using organic lip balms, but again, one with as few additives as possible is the optimal choice. Allergies to certain products, lip sticks, lip balms, and creams may cause problems for patients. This evidence is usually through trial and error to see what works for the patient. Even toothpaste allergy can affect the lips. The patient should also be questioned about other allergies, such as food, insect, or environmental-related allergies.

Portfolio Activities

- Develop your own set of skin lesion images to use as examples when talking with patients and for future reference. Consider making a permanent record of existing skin lesions of your patients for future comparison on recall appointments. Use the Mole Map, paper version, developed by the ADA to assist patients in documenting their own moles during their self-exams, available at: *http://www.aad.org/spot-skin-cancer/understanding-skin-cancer/how-do-i-check-my-skin/what-to-look-for*
- Using Clinical Protocol #10, develop a set of educational materials related to the prevention of sun damage that can be given to patients. Use self-examinations for monitoring changes in new and existing lesions. A list of dermatologists in your area should be included in the packet of materials along with a list of the Web sites mentioned in this chapter and online at thePoint.
- Have your office order/purchase a variety of skin product samples that could be given to patients seen in your office. Having an assortment of various samples of quality skin lotions with SPF, self-tanning products, and creams on hand for the patient to try provides a beneficial service. Many companies will give offices free samples to pass out to their maintenance patients. Patients are more likely to buy suggested products that are readily available, and they are more willing to try samples first. Some offices offer products such as lip balms with the office logo and number on the balm. You could then make suggestions to the patient or to the parents of children. The AAD provides such educational materials. At this time, a number of companies produce organic lip balms that are less likely to produce any skin reactions and are suitable for children.
- Your office may want to consider "Mole Mapping" to assist the patients. The company providing this service is called Digital Derm and can be viewed at *www.digitalderm.com*. The patient's mole information, size, and slide may be stored digitally on a CD to be compared at each visit.

Media Menu

Web Sites

American Academy of Dermatology
http://www.aad.org

American Academy of Dermatology: Tattoos and Body Piercings
http://www.aad.org/media-resources/stats-and-facts/prevention-and-care/tattoos-and-body-piercings

Scleroderma
https://www.scleroderma.org

Vitiligo Support Group
http://www.vitiligosupport.org/

Study Tools

Take advantage of additional online resources to help you study and ace your exams!

- Answers to case studies in the book
- Additional case studies and answers
- Interactive quiz bank with answer feedback
- Fully searchable e-book for quick lookup and studying on-the-go
- Expanded Media Menu with direct links to related Web sites and multimedia resources
- Supplemental references

thePoint Online resources and links are available at http://thepoint.lww.com/DeLong2e

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Chapter 23 **LESION/CONDITION SUMMARY TABLE**

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Basal Cell Carcinoma, Squamous Cell Carcinoma, and Melanoma	Tobacco use, heavy alcohol use, physical inactivity, poor diet, environmental agents, genetics, unprotected sun exposure, and tanning beds	Blistering sunburns cause damage to the cells and sun exposure is cumulative. Other environmental agents may make the individual more susceptible to skin cancer.	Any change in a mole or a flat macule may indicate changes at the cellular levels. Basal cell carcinoma may exhibit a round, rolled border with scaling or bleeding. Basal cell carcinoma usually occurs on the upper 2/3 of the face.	Squamous cell exhibits abnormal cells, mitotic figures, and nests of cancerous cells. Basal cell carcinoma exhibits nest of basal cells. Melanoma exhibits fine granules of melanin. Nest may be present and may invade into the connective tissue.	Surgical removal and, depending upon the extent of the cancer, chemotherapy may be needed.	A dermatologist removes cutaneous lesions and early detection is crucial. Lip involvement may cause restriction of oral opening. Any past history of skin cancer should alert the clinician to the possibility of a recurrence.
Actinic Keratosis (solar keratosis)	Previous solar exposure	UVA and UVB sun damage. This is a premalignant growth.	Scaly, dry, rough-textured patches of skin Erosion of the surface is not usually present.	Hyperkeratosis and acanthosis Rete ridges extend downward from the epithelium. A lichenoid infiltrate may be evident.	Excision and follow-up Future growths may become evident due to prior sun exposure that has damaged large areas of skin.	Actinic keratosis is a premalignant condition and calls attention to previous sun damage in the patient. The clinician should be alerted to other skin lesions in the future. Referral to a dermatologist is necessary.
Actinic Cheilitis (solar cheilitis or solar keratosis)	Previous sun damage to the lips This is a type of actinic keratosis.	Sun-loving individuals and those who work outdoors are especially prone to this type of tissue destruction. Smoking increases the risk of squamous cell due to the carcinogenic materials in tobacco.	Early loss of the vermilion border of the lip and definition of the lip is altered. Scaling of the lip is noted and may also be pigmented.	Loss of collagen and elastic fibers are noted. The epithelium is atrophic and hyperkeratotic.	Evaluation of the lips during exams is needed and referral to a dermatologist when actinic cheilitis is evident.	Since this is a premalignant condition, suggesting the use of a lip balm for all patients is needed. Note any changes and the areas may extend into the wet-line of the lip areas as well. Digital photography is an excellent way to document changes. Smoking cessation is also needed especially for those using tobacco products such as cigarettes and pipes.
Acrochordon (skin tags)	Excess skin tissue	Response to solar damage or disease process	Small areas of tissue growth May be flat or elongated	Composed of loose collagen fibers and capillaries	Excision by a dermatologist	The growths are benign but should be evaluated for changes.
Comedones	Dilated hair follicles that are filled with keratin, sebum, and bacteria	Whites more affected Solar exposure is implicated.	May appear as acne without the inflammation Dark, raised, or rough areas May resemble black heads or nevi and commonly occur on the facial areas around the eyes	Hair follicle with keratin plugs	Referral to a dermatologist and information on sun protection would be warranted.	Associated with Favre-Racouchot disease May be mistaken for common moles or nevi
Milia	Subepidermal keratinous cysts	Predisposition to developing this type of cyst	Appear on the eyelid and facial surfaces	Inclusion cysts The cyst contains eosinophilic (often laminated) keratinous substance. The cell wall appears normal.	These are benign, but with any skin problem, the patient should see a dermatologist. These cysts are often expelled with normal washing of the face.	No dental treatment issues are reported. The hygienist may be asked about the cause or prognosis of these small cysts.
Psoriasis	Plaque-like lesions that appear red, white, thin, scale-like, with a pearly surface Unknown cause	Medications, cold weather, sun exposure, and stress may exacerbate these lesions.	Usually appear on surfaces of skin that are involved in trauma such as the fingers, knees, and elbows Removal of scales may produce bleeding.	Epithelial hyperplasia is evident with acanthosis and parakeratosis. Munro microabscesses are noted.	Referral to a dermatologist	Geographic tongue has been listed as an oral manifestation of psoriasis.

continues

Chapter 23 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Rhinophyma (hammer nose)	Swollen sebaceous glands with telangiectasia Seen more in males	Increased fibrosis and vascularity	The nose may appear irregular but without ulceration. Enlarged bumps on the nose and especially the tip of the nose.	Increased fibrosis and vascularity of the tissues.	Cosmetic procedures may be performed to recontour the tissue.	Limitations in the ability to breathe in some cases may limit long appointments and the patient may need to take breaks.
Xanthelasma	Lipid material form in pale yellow plaques under the eye and usually in the corners of the eye.	May be formed due to high cholesterol levels in the patient	Flat yellow-to-orange plaques	May appear cyst-like and are composed of lipid material	Referral to a physician for cholesterol level checks and evaluation	NA
Erythema Multiforme	Multiple etiology is reported such as a reaction to a medication or contact with a pathogen.	Drug sensitivity Exposure to herpes simplex virus, mycoplasma, tuberculosis, or histoplasmosis	Target lesions and oral lesions may be present. Red "target" or "iris" lesions have a bull's eye appearance.	Lesions are not biopsied since they are clinically diagnostic.	Severe form is called "Steven-Johnson syndrome" and needs medical attention.	Dental treatment should be postponed until the EM is resolved.
Graft vs. Host Disease (GVHD)	The body recognizes the new tissue as foreign.	Side effect from organ transplant or bone graft	Loss of pigmentation that results in a spotted appearance on the skin surfaces.	Neutrophilic vasculitis, intravascular fibrin, and neutrophilic infiltrates	Patients with GVHD are at higher risk for opportunistic infections.	Patients need to have their physician treating GVHD as an intricate team member and other health care providers who may be involved including a dermatologist.
Impetigo	Staphylococcus aureus and streptococci organisms	Occurs in traumatized skin areas May be a bullous form in 30% of cases Seen in day care centers and with children in close proximity with others	Begins as an erythematous papule that becomes pustular, ruptures with a yellow, crusted appearance	NA	Highly contagious and the patient will need topical and systemic antibiotics.	Dental treatment should be postponed since the infection will spread to other areas and may infect future patients who may be seen in the practice as well.
Lichen Planus	Lichen planus is a cell-mediated immune response. Type IV	Occurs orally, cutaneous, and affects the esophageal and vaginal areas	There are multiple forms including those with classic Wickham striae in the reticular form, bullous, erosive, atrophic and plaque-like.	Infiltration of lymphocytes at the basal cell layer The BC layer becomes liquefied and definition of rete ridges is lost.	Corticosteroids are used to treat most types of lichen planus, especially those that burn, cause pain, and are erosive. A definitive diagnosis is needed and monitoring for changes is crucial since the areas have premalignant potential.	Lichen planus may affect the lips. Thinning of the tissue may be a problem. Aloe vera has been used in some cases of lip lichen planus. Careful scaling, frequent maintenance appointment, and less abrasive dental products are needed.
Lupus Erythematosus (LE)	Autoimmune disease	May affect organs in the body as a "systemic" -type lupus and may be a "discoid" type affecting the skin	Typical cutaneous lesions may be the classic "butterfly rash" found in the malar process. Scalp, eye, and oral tissues may be involved.	Lymphocytic infiltrates are dispersed about appendages and vessels. Thickened basement membrane zones	Oral and skin lesions respond to topical and intralesional corticosteroids.	Very careful scaling, elimination of harsh dental products, and a soft-bristle brush should be used. Plaque reduction and instruction in home care techniques Close contact with the physician treating a systemic lupus patient is needed for advice.

Chapter 23 **LESION/CONDITION SUMMARY TABLE** *continued*

NAME	ETIOLOGY	PATHOGENESIS	CLINICAL PRESENTATION (EXTRA-/INTRAORAL)	MICROSCOPIC/ RADIOGRAPHIC FEATURES	TREATMENT	DENTAL IMPLICATIONS
Sarcoidosis	Multisystem, inflammatory, granulomatous disease that may be associated with mycobacteria or Epstein-Barr virus	Characterized by exaggerated immune response to an unknown antigen or antigens within the organs that are affected such as the lungs and liver	All major organs may be affected. The cutaneous lesions may involve firm or spongy papular or nodular growths. The parotid gland may show enlargement.	Granulomas surrounded by an intense infiltrate of lymphocytes and multinucleated foreign body giant cells	Topical steroids manage the oral lesions.	Good oral hygiene assists in controlling the oral lesions with frequent visits every 3–4 months in some cases. Salivary gland function may be involved and xerostomia may be a problem. Managing these is of prime importance.
Scleroderma Progressive Systemic Sclerosis (Associated with: Morphea En cup de sabre CREST Sclerodactyly)	Immune dysfunction disease Classified as an autoimmune disease Some links to environmental and occupational exposure	Chronic in nature with thickening and hardening of the connective tissues May affect children and adults Abnormality in calcium salts within the tissues causing thickening and tightening of skin	Orally, with progression of the disorder resulting in fibrosis Constriction of the mouth is a concern. An inability to open the mouth or close the lips Fingers exhibit Raynaud phenomenon and sclerodactyly.	Tissue fibrosis with excessive collagen production is noted and tissues typically show a marked reduction in open blood vessels.	Medications used for blood vessel relaxation such as calcium channel blockers may be prescribed for scleroderma and Raynaud syndrome.	Careful and frequent professional cleanings and periodontal evaluations are needed. Restriction of the oral opening may make home care more difficult and assistance of special adjunctive devices may be needed. Radiographically, the clinician should be aware of widening of the periodontal ligament.
Vitiligo	Autoimmune disease Exposure to chemical substances is suspected.	Loss of pigment and/ or destruction of the melanocytes or melanocyte growth factors Breakdown in the immune surveillance system	May occur anywhere on the body and orally as well Lighter skin areas appear in a patch-like appearance. The darker the individual, the more vivid the appearance.	Loss of melanocytes or decrease in melanocytes Decreased melanin in basal cells	Medications such as calcipotriene, tacrolimus, trioxsalen, or prednisone Some patients may not need medications and may only be affected by the psychological factors related to appearance.	Advise the patient about sunscreen protection since the skin is very vulnerable in these patients. Certain facilities offer tattooing, skin grafts, topical PUVA, and laser treatments to lessen the appearance of the uneven skin tones.
Cutaneous leishmaniasis	Infection by sand flies in tropical or warm climates	Sand flies bite their hosts injecting leishmania promastigotes into the skin.	A small papule appears and increases to much bigger nodules with tissue destruction. Scars may remain due to the tissue trauma and long-term infection.	Smears are taken and the parasites may be seen in the exudates of the smear.	The patient may be given medications that treat the specific genus/parasite. Over 20 species are known. The earlier the treatment is started, the less scarring and tissue damage results.	The patient develops lifelong immunity to the specific species but may be infected by others. The face and mouth may be affected and scarring of the area can be extensive.

CLINICAL PROTOCOLS

CLINICAL PROTOCOL 1

Performing a Cytology Smear

May Be Used for Suspected HSV or Candida

Materials

- Tongue blade or spatula
- Box of glass pathology slides
- Pencil
- Can of hair spray or special fixative agent
- Mailing containers addressed to your choice of pathology labs in your area

Procedure

1. Pencil in the name of the person on the slide edge.
2. Lightly scrape the suspected area with either the tongue blade or the spatula.
3. Lightly place the scraped substance on the slide.
4. Lightly spray slide with hair spray or fixative agent.
5. Use a slide box, cardboard box, or holder for mailing that will not get damaged.
6. Mail slide to an oral pathologist for evaluation. The nearest dental school will provide the name of a facility where your cytology smear can be processed.

Courtesy of Dr. Valerie Murrah, University of North Carolina School of Dentistry.

CLINICAL PROTOCOL 2

Applying Topical Corticosteroids in the Mouth

Gel, Ointment, Cream

Your doctor has prescribed a topical corticosteroid gel, ointment, or cream for periodic application to your mouth sores. Please follow his/her instructions as written on the prescription box regarding how many times you should apply the medication daily.

It is important to make sure that one of these applications occurs just before bedtime in the evening. The medication probably stays in place longer at that time because saliva flow diminishes when you are asleep.

Whenever you can, it will help if you gently blot the mouth sores dry just before you apply the medication. Do not rub them dry; just blot using gauze. This also will help keep the medication in place for a longer period of time.

When you apply the topical corticosteroid, try to avoid rubbing it in place using a back and forth motion, because that motion may rub the "skin" surface away. Instead "dab" the medication into place.

Remember that more is not better. All you need to do is apply a thin coating of the medication. If you do this, it will stay in place better, last longer, and will be safer to use.

Rinse

Use as often as directed for as long as directed. After use, expectorate but do not ingest other liquids for 30 minutes.

Spray

Direct spray toward mouth sores as directed. After use, do not ingest water or other liquids for 30 minutes.

Prepared by Dr. T. D. Rees. From The International Oral Lichen Planus Support Group, www.tambcd.edu/lichen.

CLINICAL PROTOCOL 3

Maintenance Appointment Guidelines for the Patient with a Mucosal Disorder

- Patients should have professional cleanings every 2 to 3 months. Periodontal patients may need to be seen every 2 months, depending upon the patient's status and periodontal health.
- Careful scaling of all teeth should be performed with as little disruption of the tissue as possible. When significant periodontal pocketing is present, multiple appointments with gentle scaling and debridement are preferable to conventional deep scaling and root planing.
- All soft tissue areas should be evaluated. Findings should be described and recorded, with any suspicious areas being reevaluated. Careful evaluation for *Candida* is suggested, especially for patients who are using topical corticosteroids.

- The practitioner should note any areas that are in contact with sharp edges, crowns, or restorative materials.
- Tissue areas that do not respond to treatment may need further evaluation and possibly future biopsy.
- Ultrasonic scalers should not be used for extensive subgingival debridement to minimize irritation to the tissue.
- Polishing paste that is gritty or coarse should not be used because of irritation to the tissue both above and below the gingival margin.
- Mouth rinses containing alcohol should be avoided to prevent patient discomfort and tissue irritation.
- Air polishers are too disruptive to the tissues and should not be used.
- Any polishing of the teeth should be performed using a mild paste such as Biotene toothpaste that can be applied with a prophy cup. Simply brushing the teeth with the paste in the dental office will be of some benefit.
- For home care, recommend toothpaste without additives (such as sodium lauryl sulfate), flavor-free products, and the use of a soft bristle brush. Paste without many additives can be tolerated by most patients. It is also highly effective in patients with xerostomia.
- Patients should be instructed to discontinue the use of chewing gum, candy, mints, toothpastes, or mouth rinses that contain flavoring agents such as wintergreen, peppermint, spearmint, and cinnamon.
- Periodic oral digital photographs both for initial and for follow-up appointments are suggested. This allows better evaluation of treatment progress or lack of progress. Encourage patients to take photos on their cell phones or with their own digital camera so that the clinician has a good understanding of how the tissue responds between appointments.

Prepared by Dr. Terry Rees and Dr. Nancy W. Burkhart. Adapted from International Oral Lichen Support Group Web site, http://bcdwp.web.tamhsc.edu/iolpdallas/.

CLINICAL PROTOCOL 4

Treating Patients with Xerostomia

Salivary Glands

1. Gustatory stimulation (sugar-free candies)
2. Mechanical stimulation
   a. Sugar-free chewing gum (fruit flavors)
   b. Food (apples, carrots, celery, etc.)
3. Pharmacologic stimuli (require prescription)
   a. Salagen (pilocarpine HCl) (MGI Pharma, Inc.)
   b. Evoxac (cevimeline HCl) (Daiichi Pharmaceutical Co. Ltd.)
4. Salivary substitutes may be helpful in patients with damage of salivary glands
   a. Mouth Kote[a] (Parnell Pharmaceuticals)
   b. Optimoist[a] (Colgate-Palmolive Co.)
   c. Oral Balance (Laclede Professional Products)
   d. Salivart (Gebauer Co.)
   e. Numoisyn (Align Pharmaceutical)
   f. Oasis (GlaxoSmithKline)

Teeth

1. Maintain meticulous oral hygiene
2. Schedule frequent dental visits
3. Use prescription fluoride daily

Oral Mucosa

1. Treat oral candidiasis with oral nystatin
2. Avoid excessive use of cinnamon and mint

Prepared by Ibtisam Al-Hashimi, BDS, MS, PhD. Director, Salivary Dysfunction Clinic, Department of Periodontics, Baylor College of Dentistry.

[a] *Both contain citric acid and could potentially cause softening of the teeth. Note: Patients should also maintain adequate level of hydration.*

CLINICAL PROTOCOL 5

Diagnosing and Treating Patients with *Candida*

Initial Medical Evaluation of the Patient

1. Evaluate the patient's medical history for contributing factors to the presence of candidiasis (endocrine abnormalities, diabetes, HIV, pregnancy, etc.)
2. Perform initial dental evaluation of the patient for possible oral causative factors for candidiasis (xerostomia, poor oral hygiene, radiation therapy, aging, inadequate denture retention, etc.)
3. Evaluate symptomatology for the presence of burning or soreness of the oral mucosa, etc.

Clinical Appearance

Forms of *Candida:* Observe and note what form/forms of *Candida* may be exhibited in the patient (pseudomembranous, chronic atrophic, angular cheilitis, etc.)

Diagnostic Tools

Culturing *Candida*

1. Test tubes filled with 10 mL of diluted saline are used to culture saliva.
2. The patient rinses with the entire solution in one test-tube for 1 minute.
3. The patient expectorates all of the solution back into the test-tube.
4. The salivary specimens are sent to the microbiology laboratory for analysis.
5. Culture results are separated into three species of *Candida*.
6. Patients are notified in about 4 days of their culture results.

Exfoliative cytology

1. Roll a tongue depressor over the area of the tongue considered to be a site of candidiasis.
2. Place the specimen gathered on the tongue depressor on a microscope slide and smear the specimen on the slide evenly.
3. Fix the specimen to the slide with a cell fixative solution.
4. Write the patient's name on the frosted end of the slide in pencil.
5. Send the specimen to the pathology laboratory for staining and evaluation.

Treating Intraoral *Candida*

Various medications are used for the treatment of intraoral candidiasis. Three common medicaments include nystatin oral suspension, clotrimazole (Mycelex), and fluconazole (Diflucan). Nystatin ointment can be used at the corners of the mouth for the treatment of angular cheilitis.

Nystatin oral suspension (Mycostatin): topical agent for localized treatment for patients whose immune system is not compromised
Disp: 240 mL
Sig: 1 teaspoon four times daily for 2 minutes each time and expectorate. Use for 16 days

Mycelex tablets (clotrimazole)
Disp: 70 tablets
Sig: dissolve 1 tab on the tongue five times daily for 14 days

Diflucan (fluconazole): used for florid/disseminated candidiasis or for patients who have an immune system that is compromised
Disp: 16 tablets (100-mg tablets)
Sig: take 200 mg on day 1; take 100 mg daily for 14 days

Nystatin ointment
Disp: 15-g tube
Sig: apply to the corners of the mouth three to four times daily for the treatment of angular cheilitis

Treating Dentures

1. Chlorhexidine is an antibacterial with some antifungal properties. To use chlorhexidine gluconate 0.12%:
   Place denture in chlorhexidine gluconate solution for 1 to 2 minutes twice daily.
   Remember to treat both the denture and the oral tissues. (The denture will act as a reservoir for *Candida* and reinfect the tissues if they are not treated concurrently.)
2. Instruct patients to leave their dentures out at nighttime and to soak the denture in a 1% sodium hypochlorite solution for 15 minutes. Make sure that they completely rinse the denture under running water for at least 2 minutes before bedtime.

Prepared by Dr. Celeste Abraham, Associate Professor, Baylor College of Dentistry, TAMHSC, Dallas, Texas. Faculty in The Stomatology Center and the Department of Periodontics.

CLINICAL PROTOCOL 6

Treating Patients with Sensitivity to Flavoring Agents

Mints, gums, and candies to be avoided are those that have the various mints (mint, spearmint, peppermint) or cinnamon listed on their labels as well as the following:

Some food products containing cinnamon

Canned or packet soups
Canned meat with sauces
Curries
Chinese food
Canned vegetables in sauce
Store-made cakes or biscuits
Cola drinks
Carbonated beverages
Alcoholic drinks such as vermouth and gin
Pickles
Ketchup
Chocolates
Powdered aspirin

Toothpastes containing cinnamon

Aim
Close-Up
Regular Crest
Crest Mint
Crest Tartar Control
Colgate Tartar Control
Gleem

Toothpastes that do not contain cinnamon

Biotene
Aquafresh
Pepsodent
Colgate with MFP
Ultrabrite
Tom's Natural

Common irritants in toothpaste

Cinnamon aldehyde
Cinnamic acid
Menthol
Alcohol
Boric acid
Surfactants
Flavoring agents
Benzoyl alcohol

Carbamide peroxide
Sodium lauryl sulfate

Avoid chewing gum products that have mints or cinnamon. Some examples are

Big Red
Trident Freshmint
Trident Peppermint
Altoids Mint
Altoids Cinnamon
Ice Breakers Hot Cinnamon
Ice Breakers Cool Mint

Benzoates (benzoic acid, sodium benzoate, propyl 4-hydroxybenzoate) are preservatives found in foods, carbonated beverages, sauces, fruit products, and toothpastes. They can cause reactions in the oral mucosa similar to those of cinnamon-containing products. Most toothpastes contain benzoates; some toothpastes that have no benzoates are Crest and Macleans Fresh Mint.

There are several steps to take when you have a patient whom you suspect has sensitivity to various flavoring agents found in toothpastes, mouth rinses, gums, and food products.

Elimination diets, keeping a food diary, as well as patch testing and intraoral biopsies are important in ruling out allergies to flavoring products. Patch testing is useful to distinguish irritant reactions from allergic reactions.

1. It is advisable to first remove/eliminate the causative agent, if that agent is known.
2. The use of intraoral topical steroids may be required.
3. Patients may be referred to a dermatologist for the evaluation of possible skin disorders and for patch testing. Patches with the suspected allergen are placed on small disks and evaluated at intervals of 48 and 72 hours. The results are evaluated as doubtful, weak, strong, or extreme reactions.
4. Patients may be advised to avoid foods that irritate the mouth, such as spicy foods that may contain preservatives such as cinnamon.
5. Patients may be advised to avoid soft drinks, candies, mints, and chewing gums in case allergy to flavoring agents is suspected.
6. Patients may be asked to keep a food diary and list all the foods that they ingest over a period of 1 to 2 weeks. They must also list the dentifrice they are using, any snacks that they may eat between meals, any alcoholic beverages they drink, etc.
7. A biopsy to rule out other oral lesions may be required if there is no resolution after a few recall appointments.

Prepared by Dr. Celeste Abraham, Associate Professor, Baylor College of Dentistry, TAMHSC, Dallas, Texas. Faculty in The Stomatology Center and the Department of Periodontics.

Adapted from handouts of the Stomatology Center, Baylor College of Dentistry, Dallas, Texas and from the handbook Non-plaque-related Diseases of the Periodontium *(Terry D. Rees, 2005).*

CLINICAL PROTOCOL 7

Patient Education: Recommendations for Recurrent Herpes Labialis

Proper diagnosis of recurrent herpes labialis (RHL) is important to help with treatment and prevention. A diary of the nature of the outbreak can help identify a triggering event. Location, appearance, symptoms such as duration, type and severity of pain, exposure to cold air, sun, stress (emotional or physical), types of dental treatment, fever and infections, and, in some cases, allergies are helpful elements to include.

- Itching, tingling, or burning may precede the eruption of vesicles. The reactivation of the virus from the nerves occurs repeatedly in the same location. It is rare that a patient has RHL in more than one area.
- Typically, there is a cluster of vesicles as the virus comes to the surface. The surface of the vesicle ruptures easily within several hours, leading to a weeping of fluid that contains virus particles and can spread the infection to the patient's partner or other sites. The area then progresses to a crust or scab, with or without bleeding. Most patients heal within 7 to 10 days of the vesicle formation.
- Topical antiviral cream (1% penciclovir) or ointment (5% acyclovir) are helpful for some patients. Patients should apply the ointment to the area every 2 hours while awake. For some patients, this may prevent the vesicle formation. In others, it reduces the duration and may make the lesions less infectious (patients should continue application every 2 hours for up to 1 week). These prescription topical agents also keep the crust moist and flexible so it is less likely to crack and bleed, and, therefore, is less painful.
- Over-the-counter docosanol 10% (Abreva, GlaxoSmithKline) helps some patients. Patients should apply this agent to the area five times daily until healed.
- Patients should wash hands frequently and always after manipulation of these areas. A cotton tip applicator may be helpful to apply the cream or ointment. Some preparations come in a tube with a narrow applicator tip that allows more precise placement, but the tube should be discarded after the episode so as not to infect another area.
- The systemic antiviral valacyclovir has been approved to prevent RHL. Eight 500-mg tablets should be prescribed. Patients should be instructed to take four tablets when the first symptoms are noticed; they then should take four tablets 12 hours after the first dose is ingested. This is a very time-sensitive prescription and patients should have the tablets in their possession; this usually is only prescribed for patients who have had a clear history of recurrence, with episodes that occur more than six times per year.
- Use of lip balm with SPF 15 sunscreen or higher may help patients whose episodes are stimulated by sun exposure.

- Routine dental treatment should be deferred during the vesicle and crust stages, for the patient's comfort as well as for reducing the spread of infection. Proper infection control is essential to protect the clinician as well as other patients.

Prepared by Dr. Wendy S. Hupp, DMD, Assistant Professor of Oral Medicine, Department of Diagnostic Sciences, Prosthodontics, Restorative Dentistry, University of Louisville School of Dentistry

CLINICAL PROTOCOL 8

Treating Patients with Intraoral Ulcers (Recurrent Aphthous Ulcers, Traumatic Ulcers, or Recurrent Intraoral Herpes)

Understanding the cause of intraoral ulcers helps to prevent recurrences and to select the best treatment. A diary of the nature of the ulcer helps to distinguish between aphthous and traumatic ulcers (TU) and recurrent herpes. Information that is helpful to determine the diagnosis includes location; appearance; symptoms such as duration, type, and severity of pain; and "triggers" such as cold air, sun exposure, stress, dental treatment, fever and infections, and, in some cases, allergies. All patients who have intraoral ulcers may choose to defer dental treatment until they are more comfortable.

Recurrent aphthous ulcers

- Recurrent aphthous ulcers (RAUs) usually start to appear in the teen years and most commonly are solitary round or oval lesions on movable tissue; they have a red halo and a yellow to white covering, are quite painful, and heal within 2 weeks without scarring.
- RAU may be more frequent in patients during high stressful periods, such as during a woman's menstrual period or during an emotional situation.
- RAU are caused by the immune cells called T lymphocytes that lead to a limited destruction; therefore, treatment should include some type of immune modulator, such as topical steroids (see Clinical Protocol #2). In some patients, the early use of steroids can actually prevent the RAU from becoming very severe, but overuse of topical or systemic steroids may lead to candidal infection or medication side effects.
- Palliative treatment should be suggested for patients to help manage the symptoms. Warm saline and bicarbonate rinses are helpful: ½ teaspoon of table salt and ½ teaspoon of sodium bicarbonate (baking soda) in 8 oz of warm water, swished and held in the mouth until the warmth dissipates, and then expectorated. This can be used after meals in place of tooth brushing during the most painful time. Another product called Orabase Soothe-N-Seal (Colgate, no prescription needed) works for up to about 6 hours. It is similar to super glue and helps by covering up the nerves, even providing some protection from further injury. It is likely that this coating allows the ulcer to heal a little faster. Other topical anesthetics may be too caustic; while easing the pain, they may actually delay healing. Viscous lidocaine mixed with diphenhydramine elixir and an antacid liquid such as Maalox (Novartis Consumer Health) or Kaopectate (Pfizer Consumer Healthcare) can also be used. The pharmacist must mix these three liquids in equal parts, then the patient can swish a teaspoonful for 30 to 60 seconds and spit before meals. Caution the patient that this may lead to difficulty swallowing because the mouth is numb.

Traumatic ulcers

- TU can occur at any time and anywhere in the mouth, but can be confused with RAU when they are present on movable tissue. They are usually linear or with irregular edges, with a yellow to white covering, and variably with a red halo.
- Trauma occurs from broken fillings or rough edges of teeth, extreme temperatures (e.g., hot food or drinks, very cold foods), eating implements, misuse of medications (e.g., an aspirin tablet applied to the tissue or overuse of topical anesthetics), or other chemicals that may cause burns or allergic reactions. A food diary is helpful in diagnosing some patients, including use of any toothpaste, mouthwash, bleaching products, chewing gum or candies, and condiments such as cinnamon that are placed into the mouth.
- TU may heal faster with the use of topical steroids once the cause is removed.
- See palliative treatment above.

Recurrent intraoral herpes

- Recurrent intraoral herpes occurs on nonmovable tissue, most commonly on the hard palate in the premolar region (see section on Herpes Labialis). There is a clear demarcation at the midline as the virus follows a nerve, and the same area is affected repeatedly.
- Dental treatment is commonly the stimulus for recurrence, including injections and tissue manipulation during scaling and curettage.
- Vesicles are often missed because the covering is very delicate; the ulcerations that follow are shallow and multiple, but may coalesce to form a larger, irregularly shaped lesion that has a yellow to white covering and a red halo. These lesions often become painful, but the patient may confuse the pain with that of the dental treatment that initiated the recurrence.
- Recurrent intraoral herpes is best treated by prevention, perhaps with systemic antiviral medications just before the manipulation of the tissue. Topical antiviral preparations are not helpful. At the first sign of itching, tingling, or burning, valacyclovir 2,000 mg should be taken, repeating the same dose 12 hours later. This 1-day treatment is also used to treat RHL.
- Once the ulcers have occurred, the same palliative measures for RAU and TU can be used (see above). Topical steroids should not be used for herpetic lesions in the early stages.

Prepared by Dr. Wendy S. Hupp, DMD, Assistant Professor of Oral Medicine, Department of Diagnostic Sciences, Prosthodontics, Restorative Dentistry, University of Louisville School of Dentistry.

CLINICAL PROTOCOL 9

Preventing Further Oral Tissue Damage in Patients with Eating Disorders

- Carefully monitor the amount of enamel loss by using models and intraoral photographs.
- Provide patients with custom trays and 1.1% neutral fluoride gel (Prevident[a]). Patients can use the trays for 5 minutes daily. A good time is while taking a shower.
- After vomiting, rinsing with 1 teaspoon of baking soda mixed with 8 oz of water will help neutralize the hydrochloric stomach acids that damage the enamel.
- Daily rinses with 0.05% fluoride (such as Act[b]) will help harden the enamel against acid dissolution.
- Rinse with just water after vomiting (if baking soda and water is not available).
- Do not brush the teeth for at least 1 hour after vomiting. Rinsing after vomiting is crucial to minimize enamel loss.
- Instruction on proper tooth brushing methods using a soft-bristle toothbrush is important to minimize enamel loss.
- Instruct patients on use a tongue cleaner and to brush the tongue thoroughly to remove acid residue that collects in the papillae after vomiting.
- Encourage patients to drink water throughout the day to decrease the acid content of the mouth.
- Minimize the use of abrasive materials in professional dental hygiene procedures related to scaling and polishing practices.
- Providing education for healthy snack foods is crucial. Foods such as cheese, fruits, vegetables, and other nonacidic, non–sugar-containing foods are important to good oral and general health.
- Encourage saliva flow with the use of sugarless gum and mints, especially those sweetened with xylitol.
- Suggest that patients drink through a straw when drinking any acidic beverage such as fruit juice or carbonated beverages.

Adapted and modified from Burkhart, N. Roberts M, Alexander M, Dodds A. Communicating effectively with patients suspected of having bulimia nervosa. J Am Dent Assoc 2005;136:1517.

[a]*Colgate Oral Pharmaceuticals, Inc.*

[b]*Johnson & Johnson Distributed by Personal Products Company. Division of McNeil-PPC, Inc., Skilman, New Jersey.*

CLINICAL PROTOCOL 10

Patient Education: UVA/UVB Skin Protection

- Sun avoidance is the best defense. Remember that sunscreens reduce the damaging effects, but do not eliminate them.
- Use a broad-spectrum protection sunscreen of at least an SPF 30 (sun protection factor) and apply approximately 1 oz, 20 to 30 minutes before going out into the sun. A measurement device equivalent is a shot glass or a "golf ball size" portion.
- Apply every few hours, and always reapply after going in water. When going in the water, use a waterproof sunscreen and reapply after 50 minutes, if you have been in the water for that amount of time. Reapply if you perspire a lot. Do not assume that a higher SPF will protect you much longer than a lower one (i.e., SPF 30 vs. SPF 50). There is only a slight variation in the protection abilities. Reapplication is always crucial. Sprays wash off more readily and water dissipates the sunscreen.
- Ultraviolet B (UVB) light is primarily responsible for tanning and burning. Ultraviolet A (UVA) is light that penetrates deep into the tissue.
- Active ingredients of a sunscreen should contain titanium dioxide or zinc oxide. Titanium dioxide and zinc oxide protect against both UVB and UVA exposure. Some sunscreens may have harmful ingredients, so be a wise and informed consumer.
- Be aware that concrete, snow, and water can reflect up to 85% of the sun's rays, exposing you to more than double the normal amount.
- Seek shade between 10:00 AM and 4:00 PM. This is the time when the ultraviolet light is the most intense. Even cloud cover allows 80% of UV rays to pass through. The UV Index is on a 0 to 10+ scale, and special care should be taken when the index is 5+. Remember that the shorter your shadow, the more damaging the sun's rays.
- Wear a wide-brimmed, tightly woven hat that has been specially treated to block the sun's rays. Wear opaque clothing specially treated to protect the skin (one that has a UPF [ultraviolet protection factor] of 30 or more), and buy large beach umbrellas that are specially protected to block the sun's rays completely at 100%.
- **Never** use tanning beds—the exposure emits mostly UVA rays, which penetrate deeply into the tissues, causing considerable tissue damage, premature aging and significantly increases your risk for cancer. Deadly melanoma is increased with use of these facilities. Younger individuals are especially susceptible to UVA damage and the damage caused by tanning beds. Cells are rapidly dividing and mutations occur. Most tanning beds are not regulated, and body parts such as the genitals that are not normally exposed to the sun receive radiation. Often the eyes may be exposed as well since many consumers remove the glasses to avoid white circles in the eye area. Consider using sunless self-tanning lotions. Do not use spray on tanning products administered in tanning salons because the vapors that are inhaled may result in lung damage.
- Use a lip balm containing PABA (para-aminobenzoic acid) as an active ingredient and at least an SPF of 15. Some lipsticks now contain sunscreen as clearly stated on their labels.

- Wear sunglasses with wraparound frames that have total UV-blocking capacity. Avoid metal frames. Metal frames intensify the damage from the sun. The eye area is a prime location for basal cell carcinoma due to the sun's damage on the skin.
- Know the ABCDEs of skin cancer.
- Perform skin self-exams monthly using a hand mirror and search for any skin spot that has changed color, size, or shape. The American Academy of Dermatology's (AAD at http://www.aad.org/) mole guide is a great resource.
- Ask your hair salon or stylist to check the scalp and hairline for any discoloration or lesions while shampooing your hair.
- Melanoma may occur on the nails of both the hands and feet. Look for any discoloration or streaks within the nail bed.
- Be evaluated by your dermatologist at least once a year or every 6 months if you have a history of skin cancer, especially melanoma. Always make an appointment for any new noticeable growths or changes in your skin.
- Cloudy days do not protect you from sun damage, dark skin does not protect you, and a good tan does not protect you from further damage. Protect yourself while driving, flying, and in the office. The damaging rays still come through windows.
- REMEMBER THAT EARLY DETECTION IS THE KEY!
- SEE YOUR DERMATOLOGIST YEARLY OR EARLIER FOR CHANGES.
- NEVER GET SUNBURNED—THIS IS THE BEST DEFENSE. Teach children good skin care—PASS IT ON! IT LASTS A LIFETIME.

Prepared by Dr. Nancy Burkhart, RDH, MEd, EdD, 2012.

CLINICAL PROTOCOL 11

Patient Education: Oral Cancer Self-Examination

1. When you perform your intraoral examination, give the patients a large mirror and show them what you are seeing. Point out the normal anatomy and any atypical findings that you may see so they will know what is normal for them (e.g., benign migratory glossitis, Fordyce's granules, and tori or exostoses).
2. Instruct patients they are looking for any of the following signs or symptoms of cancer. In most cases, these symptoms should be present for approximately 2 weeks; however, anything that a patient is concerned about should be brought to the attention of a medical or dental professional as soon as possible.
   - Sore in the mouth or on the lip that does not heal (the most common symptom)
   - Red or white patch on any oral tissues, tongue, tonsil, or lining of the mouth
   - Irritation, lump, or thick patch in the mouth, neck, or throat
   - Persistent sore throat, or a feeling that something is caught in the throat
   - Hoarseness or change in the voice
   - Numbness in the tongue or mouth
   - Pain or bleeding in the mouth that does not resolve
   - Difficulty chewing, swallowing, or moving the jaws or tongue
   - Ear and/or jaw pain
   - Chronic bad breath
   - Changes in speech
   - Loosening of teeth or toothache
   - Dentures that no longer fit
   - Unexplained weight loss
   - Fatigue
   - Fever of unknown origin, especially when prolonged; this is usually a sign of paraneoplastic syndromes and indicative of advanced disease.
   - Loss of appetite, especially when prolonged (anorexia); similar to fever, this is usually a sign of advanced disease.
3. The following are suggestions for instructing the patient how to do the self-examination:
   - Find a mirror in a well-lighted area; do not use a mirror that you need to hold unless you have no other option.
   - Have a flashlight with a strong beam available for use.
   - Start by directing the flashlight beam toward the back of the throat by bouncing the light off of the mirror into the throat area.
   - Look at the roof of the mouth.
   - Stretch the cheeks out from the teeth and look at the lips.
   - Put the tongue on the roof of the mouth and look at the floor of the mouth.
   - Stick the tongue out or hold it and look at the top, both sides, and the bottom.
4. Any suspicious findings should be brought to the attention of a medical or dental professional. The self-examination should be preformed once a month.

The continuing education course "Promoting the Patient Oral Self-Assessment" is an excellent resourse for the dental hygienist and can be found on Dentalcare.com. Course #347 *http://www.dentalcare.com/en-US/dental-education/continuing-education/continuingeducation-landing.aspx*

Prepared by Leslie DeLong, RDH, MHA.

CLINICAL PROTOCOL 12

Adjunctive Oral Premalignant Screening Devices

The essential part of any form of early detection begins with the clinical exam of the patient, including a careful assessment of the health history, a lifestyle factor evaluation and,

ultimately, the extraoral and intraoral dental exam. Dental students and dental hygiene students are taught that the clinician must search for an explanation for any persistent lesion that appears to be of abnormal color or size, or exhibits any unusual characteristics. A dilemma develops when a lesion is detected that does not appear to be threatening, but that also has no known etiology. Lesions such as this may be associated with an injury or a benign condition, or they may contain dysplastic cells and be the clinical manifestation of the early stages of premalignant or malignant growth. The newest cancer screening devices/techniques in combination with basic knowledge of oral pathology and disease mechanisms can potentially help the clinician identify lesions that have a higher degree of suspicion and, therefore, present with a more urgent need for a definitive diagnosis. These devices/techniques are considered to be screening adjuncts to, not substitutes for, a tissue biopsy that will result in a microscopic diagnosis. They should help the clinician and the patient with their decision to either: (1) proceed with a referral, (2) perform a biopsy, or (3) monitor the lesion. However, it should be noted that, while a report that is positive for dysplasia or malignancy in a high-risk site indicates the immediate need for a biopsy, a negative report does not mean that the lesion is necessarily innocuous, and should result in the clinician and the patient more closely monitoring the lesion for no evidence of clinical change or symptoms for at least the next 2 years.

Exfoliative Cytology

Exfoliative cytology has been performed for many years. It is the basis for the Pap test women are familiar with and it has been used in the oral cavity to help determine if a biopsy is necessary albeit with mixed success due to high false-positive and false-negative rates. Historically, this procedure was performed with a moist tongue depressor or cotton tip applicator that scraped surface eptihelal cells off the lesion. In 1999, a technique using a patented spiral stiff nylon bristle brush was introduced, and termed "the brush biopsy." A few years ago, this test was renamed the BrushTest.

Brush Biopsy (BrushTest™)

Materials for performing the "brush biopsy" are obtained from the company that developed and markets the system, and that will eventually examine the specimen and report the findings to the dentist.

Materials in the kit include:

- Brush
- Clear glass slide with bar code identification
- A fixative liquid contained in a sealed pouch
- Plastic slide container for protection of the slide during transport
- Bar coded requisition form for patient, lesion, and billing information
- Mailer box for return of the specimen.

Procedure

- The cells for the specimen are obtained by twirling a patented spiral-shaped, stiff nylon brush into the lesion.
  - Enough pressure is applied to the lesion that a slight bend appears in the brush's shaft.
  - Continue to twirl the brush on the lesion until pinpoint spots of bleeding are observed. This should be done to indicate that cells from the entire thickness of the epithelium (i.e., transepithelial) have been gathered in the specimen.
- Transfer the collected cells immediately to the slide provided in the kit. The surface of the brush that was used to obtain the sample should be rotated onto the slide. Continue to rotate the brush on the slide until an observable film is seen on the surface of the slide.
  - If no film is seen, repeat the technique on the lesion with the same brush.
- Apply the liquid fixative to the slide immediately after you have determined that you have an adequate sample. Do not worry about excess fixative that runs off the slide. Let the slide dry for approximately 15 to 20 minutes.
- Place the slide in the container provided and follow the instructions to submit the sample for testing.

Liquid-Based Cytology

A relatively new cytology technique is being used by many hospitals and obstetrics-gynecological practices in place of the traditional scraped Pap smear. The technique may also be used to collect oral specimens. A cytology brush with nylon bristles is used to collect a sample of cells, but instead of transferring the cells onto a glass slide as in a traditional Pap smear or BrushTest, the brush is twirled in a container that holds an alcohol-based fixative/preservative liquid. By using this method, many of the harvested cells are available for analysis. Following collection, the plastic cytology brush's shaft is twirled in the liquid container and then is cut so that the brush head is also placed in the container. The preservative liquid container with the collected cells and brush head as well as a requisition form is sent for testing. Peer-reviewed medical literature reports that this technique yielded a better representative collection of lesional cells. In addition, the cells to be studied are filtered from unwanted debris included in the sample resulting in a reportedly qualitatively superior slide for microcopic examination. This procedure has been shown to decrease the false-positive and false-negative reports observed with the traditional exfoliative cytology technique in a gynecological setting.

Toluidine Blue Vital Staining

This technique was first introduced in the early 1970s with varying degrees of acceptance and has been used more or less ever since. It recently has been the object of several

studies, and its use appears to be increasing once again. Toluidine blue is a basic metachromatic vital dye that stains the DNA nuclear material of cells that are undergoing increased DNA synthesis, such as dysplastic, malignant cells and atypical reactive cells (from inflammation). The stain is being used to help determine a degree of suspicion with regard to a specific lesion and, in some cases, guide clinicians in determination of the best biopsy site for maximum diagnostic yield (i.e., a marker system).

Materials

- 1% toluidine blue dye
- Water
- 1% acetic acid solution

Procedure

- Rinse the mouth with water twice, for approximately 20 seconds each time, to remove debris.
- Rinse the mouth with 1% acetic acid solution, for approximately 20 seconds, to remove saliva.
- Gently dry the area.
- Apply the toluidine blue dye to the high-risk areas or to a specific lesion.
- Rinse with 1% acetic acid for 1 minute to clear excess stain.
- Rinse with water.

Interpretation

Expertise is required to interpret positive retained staining (i.e, royal navy blue) from inconsequential diffuse, light blue film or mechanical retention of the stain (e.g., filiform papillae of the tongue). This procedure is more than 90% accurate in identifying lesions that are dysplastic or malignant.*

Chemiluminescence (Vizilite® Plus, Zila Pharmaceutical, Phoenix, AZ)

The two-part system uses an endothermic chemical reaction blue lightstick to help identify abnormal areas and toluidine blue (i.e., tolonium chloride) to mark these areas.

Materials

- Small bottle of 1% raspberry-flavored acetic acid solution (vinegar)
- Activated chemical lightstick
- Toluidine blue dye (TBlue630®)

Chemiluminescent Procedure

- Rinse the mouth with the acetic acid solution for 1 minute and expectorate.
- Activate the light source by breaking the inner vial and shaking the capsule to mix the chemicals.
- Assemble the light source's plastic holder and place the activated light source within it.
- Dim the ambient room lights and look for white-appearing lesions or areas.

Interpretation

- Normal epithelium absorbs the device's light and appears dark.
- Abnormal cells will reflect the light and appear white.
- Once the suspicious areas are identified, you can mark these areas with the supplied toluidine blue dye for subsequent incisional or excisional biopsy.

Precautions

- ViziLite® Plus should not be used for pregnant women or children. Other precautions are noted in the manufacturer's instructions.

Direct Optical Fluorescence Visualization Technology (VELscope VX™)

The VELscope™ VX is the newest version of this company's technology—a handheld unit emits a safe blue wavelength of light into the mouth, which stimulates fluorophores within the surperficial mucosa tissues, causing them to emit a dim fluorescent green glow. Special optical filters within the device allow the clinician to directly view the different fluorescence responses of healthy versus abnormal oral tissue.

Materials

- VELscope™ handheld unit, infection-control plastic sleeves, and screw-on front caps.

Procedure

- Turn off ambient lights, turn on the handheld unit, and direct the light at the oral tissues, directly observing the fluorescence response through the filtered eyepiece.
- Healthy oral mucosal tissue will appear bright green while suspicious regions are identified by a loss of fluorescence (i.e., appear dark).

Identafi 3000 Ultra™

The portable, AA rechargable battery-operated Identatfi™ aluminum-plated handpiece emits a safe violet wavelength of light into the mouth, which stimulates the fluorophores with the superficial mucosa tissues, causing them to emit a fluorescent blue glow when viewed with special optical filter glasses. The light source emits next to a disposable plastic sheath with an attached angled examination mirror. As with the VELscope, this device allow the clinician to view the different fluorescence responses of healthy versus abnormal oral tissue. The device also has a white light setting and an amber light setting. The wavelength of the latter, according to the manufacturer, allows the clinician to evaluate the vasculature feeding the suspcious area to help reduce false positives.

Materials

- Identafi 3000 Ultra handpiece/unit
- Patient protective eyeglass and clinician filtered eyeglasses
- AA battery recharger

Procedure

- Turn off ambient lights and direct the unit light at the oral tissues, observing the fluorescence response, while wearing the supplied filtered glasses.
- The healthy oral mucosal tissue will appear bright green, while suspicious regions are identified by a loss of fluorescence and will appear dark.

DentLight D.O.E.™

The portable, lithium rechargable battery-operated handpiece emits a safe blue wavelength of light into the mouth, which stimulates the fluorophores with the superficial mucosa tissues, causing them to emit a fluorescent green glow when viewed with special flip-down optical filters with supplied optical loupes. The handpiece utilizes the manufacturer's composite curing light (Fusion®) with a removal attachment head. Both a white light and blue light attachment come with the kit. The handpiece has a LCD display with variable activation timer (range 5 to 20 seconds in 5-second increments and a manual mode). Note: If the clinician already owns the Fusion light curing system, then the two additional attachments can be purchased at a reduced price.

Materials

- DentLight unit
- Patient protective eyeglasses
- Combination base/recharger unit
- Loupes with paired flip-down filters

Procedure

- Turn off ambient lights and direct the white light, and then the blue light, at the oral tissues, observing the fluorescence response with the latter, while wearing the supplied filtered loupes.
- The healthy oral mucosal tissue will appear bright green, while suspicious regions are identified by a loss of fluorescence and will appear dark.

**From Silverman S, Migliorati C, Barbosa J. Adjunctive techniques in oral cancer detection. Dimensions of Dental Hygiene 2006;4(9):28.*

Prepared by Dr. Michael Kahn, Chairman and Professor of Oral and Maxillofacial Pathology, Tufts University School of Dental Medicine, 2012.

CLINICAL PROTOCOL 13

Alleviating the Oral Symptoms of Mucositis

Patients undergoing chemotherapy or radiation therapy for cancer or for other conditions associated with the development of mucositis should be examined by a dental professional prior to the start of therapy. All possible measures should be taken to prepare the patient's mouth for therapy by eliminating existing infections and sources of trauma (e.g., sharp restorations), and to educate the patient about the oral effects of the proposed treatment. Patients should be advised about what to do when and if they have painful oral lesions and they should have written instructions and access to medications and products for managing mild pain at the very least. Therapy for alleviating painful mucositis should be based on the level of pain present and will be different for every individual. The following suggestions may be used as a starting point for managing the patient with pain from oral mucositis in consultation with the patient's oncologist or other physician.

1. Remove any prosthetic appliances during episodes of mucositis.
2. For lesions that do not resolve, evaluate the patient orally for a secondary bacterial or yeast infection.
3. Keep the oral tissues moist in the presence of xerostomia (refer to Clinical Protocol #4).
   - Increase fluid intake.
     - Sip on water frequently.
     - Suck on ice chips.
   - Use sugar-free candy or gum (products containing xylitol are excellent for stimulating saliva and inhibiting the growth of oral bacteria).
4. Use bland oral rinses to soothe tissues and maintain hydration. Avoid any rinse containing alcohol or other astringents. Use 12 to 16 oz every 6 hours or as often as every 15 to 30 minutes. Use rinses prior to using medicated rinses or applying topical medications or anesthetics to remove saliva and debris.
   - Saline solution: ¼ teaspoon salt, 8 oz water—helps moisturize tissues, reduce irritation, and removes thick saliva and debris
   - Sodium bicarbonate: 1 to 2 tablespoons baking soda in 32 oz water—neutralizes acids after vomiting, dissolves thick saliva, soothes tissues, and dislodges debris
   - Combined saline/bicarbonate rinse: saline has a slightly acidic pH, adding bicarbonate makes the rinse neutral or very slightly basic pH.
5. Use topical anesthetics and/or systemic pain medications for pain control.
   - Topical anesthetics should be used as soon as possible to manage mild to moderate pain and should continue to be used in conjunction with systemic pain relievers for moderate to severe pain.
   - Avoid accidental mucosal injury.
   - Avoid using on the soft palate or rear of the mouth.
   - Do not eat or perform oral hygiene procedures while anesthetized.
   - *Examples*:
     - Lidocaine: viscous gel, jelly, ointment, solution
     - Benzocaine: gel, ointment, spray
     - Tetracaine/Chirocaine: anesthetic tablets

- EMLA: lidocaine and prilocaine mixture
- Compounded rinse (Magic Mouth Rinse): lidocaine, Benadryl, Amphojel, nystatin, and sometimes a topical steroid. The ingredients in these rinses vary according to the individual prescriber.

6. Systemic analgesics: mild analgesics should be used at the onset of discomfort with stronger medications offered if the level of pain increases.
   - Mild pain
     - Nonsteroidal antiinflammatory drugs
     - Acetaminophen
     - Ibuprofen
     - Naproxen
     - Nonselective COX-1 and COX-2 inhibitors and selective COX-2 inhibitors
     - Opioids
     - Codeine
     - Oxycodone
   - Moderate to severe pain
     - Morphine
     - Oxycodone
     - Methadone
     - Fentanyl

Prepared by Leslie DeLong, RDH, MHA. Used with permission from Rankin KV, Jones DL, Redding SW, eds. Oral Health in Cancer Therapy, third edition. Texas Cancer Council, 2008:43–57.

CLINICAL PROTOCOL 14

Postoperative Instructions for Oral Surgery Patients

You have just had a dental extraction, an oral surgery procedure. The following instructions, which may be modified by your doctor, will help you recover from this procedure as you heal over the next several days:

1. Bleeding: Applying firm pressure, continue to bite on the gauze pack for an hour. Do not chew on the packing; if you have to talk, do so with clenched teeth. At the end of an hour, remove the gauze and, if you are still bleeding or oozing, replace it with gauze that has been given to you, biting on it for 30 minutes. If bleeding still persists, wrap a tea bag in fresh gauze, moisten it, and bite on it for another 30 minutes. If this does not solve the problem, call the office or go to a hospital emergency room.
2. Rinsing/spitting: Do not rinse or spit for the rest of the day. This is very important, as rinsing or spitting can dislodge the clot, causing renewed bleeding and other complications. Just swallow instead; you will be swallowing the same saliva you have been swallowing for years. You may swallow a little bit of blood that is mixed with the saliva; don't worry about it, it won't hurt you.
3. Swelling: Use an ice pack to minimize swelling, 20 minutes on and 20 minutes off for the rest of the day. You can easily make an ice pack out of a bag of frozen peas: just bang on the bag to loosen the peas, then wrap it in a towel and apply it so it molds to the side of your face. Do not use ice for more than 24 hours, and never apply heat to your face unless your doctor tells you to.
4. Medication: You may take over-the-counter medication that you usually take for pain, and your doctor may have prescribed a stronger medication, such as a narcotic. The sooner you take pain medicine after surgery, the more effective it will be. Try to take it at regular intervals, before your pain returns, so you remain as pain-free as possible during the postoperative period. Always swallow the medication; do not let it dissolve in your mouth next to the surgical site. You may also have been prescribed an antibiotic. Take it as directed, and try not to miss any doses. If you do miss a dose, do not double up; just take the missed dose as soon as you remember it, then resume the prescribed schedule. (See "A word about antibiotics" at the end of these instructions.)
5. Eating: After you remove the gauze, and there is no more bleeding, you may eat anything you desire on the other side of your mouth. For the first few days, you may be more comfortable eating soft foods such as cool soup, applesauce, mashed potatoes, baby food, milkshakes, yogurt, ice cream, etc. It is important to maintain a good nutritional intake, as this is essential for rapid and proper healing. Do not worry if you accidentally chew on the extraction side; you will not do any damage, as your body will quickly remind you of your recent surgery.
6. Drinking: Avoid drinking through a straw, especially if you have had an upper back tooth removed. Sometimes the roots of these teeth are very close to your sinuses, and drinking through a straw can cause complications. Your doctor will tell you if other precautions are necessary.
7. Smoking: Above all, if you smoke, DO NOT SMOKE for at least a week after surgery. If you had an open wound on your hand you wouldn't blow smoke into it, would you? Similarly, you now have an open wound in your mouth, and your body needs all the tender loving care you can give it to help you heal. Don't make its job harder by smoking!
8. Oral hygiene: It is imperative that you keep your mouth clean. Starting this evening, brush and floss your teeth as you normally do, but avoid the surgical site; and remember to rinse the toothpaste from your mouth very gently with a small amount of cool water. You should be able to resume brushing the surgical area within a day or two. If it hurts to brush gently, just cleanse the area with a moistened gauze pad.
9. Irrigation: Starting tomorrow, rinse your mouth with warm salt water. This is one of the most important things you can do to help you heal and feel better as soon as possible, and you can't do it too often! Rinse as follows: fill an 8-oz drinking glass with very warm

water and stir in half a teaspoon of table salt. Rinse with a small amount of this mixture, bathing the surgical site. Be gentle; it is not necessary to rinse vigorously. When the water cools off, spit it out and take another portion. Do this until you have used up the entire glass. Repeat every 2 hours while you are awake, and continue for 3 to 5 days.

10. Sutures: Your doctor may have placed sutures (stitches) over the surgical site to enable your body to heal faster. If the sutures are made of a resorbable material ("gut"), they will dissolve in 7 to 21 days, depending on the type used, and you should not need a follow-up visit. If a nonresorbable suture was used (silk, nylon, etc.) you will have been given an appointment to return to the office in 5 to 7 days to have them removed. This will also give your doctor a chance to check on your progress, so it is imperative that you keep this appointment.

A word about antibiotics: If you have been given an antibiotic, it is very important that you take it as directed to treat your infection caused by "bad" bacteria. Antibiotics must be taken regularly, usually every 6 hours by the clock, and should be taken until they are all gone. Do not share them with anybody else, and do not save some for another time. Antibiotics may cause gastrointestinal (GI) distress, which can be avoided by eating a cup (4 to 8 oz depending on the container) of yogurt, 20 to 30 minutes after each dose. It doesn't matter what brand or flavor of yogurt you choose; it can be with or without fruit; fat-free or not. What's important is that it has live cultures, and it will say "with active cultures," or "with live cultures" on the package. Do not use yogurt that is sterilized or does not have the "culture" statement on the package-it will not protect you from GI distress! The reason for this is that antibiotics, as they go through your GI tract, can destroy the "good" bacteria needed for proper digestion, and if these are not replaced you may experience distress (pain, gas, diarrhea). The live cultures replace the good bacteria that are normally present. Some antibiotics are more likely to cause distress than others, but if you have been prescribed clindamycin or Cleocin ® (Pfizer, New York, NY), it is very important to eat the yogurt, as described above, after every dose. Your doctor will advise you of any additional precautions concerning antibiotics or any medicine prescribed for you.

Good luck with your recovery! These instructions were written with your welfare and comfort in mind. If you follow them carefully, you will minimize postoperative problems. If you have questions or concerns, experience swelling or severe pain after the 2nd day, or develop a fever over 101°F, do not hesitate to call the office. If it is after hours, your doctor or a doctor-on-call can be reached through the answering service.

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CLINICAL PROTOCOL 15

Office Protocol for Identifying Suspected Family Violence

REMEMBER—Office safety planning must be a part of the office protocol before any intervention in suspected family violence.

Steps in Identification of Suspected Family Violence

1. **General physical assessment of the patient.** Although general physical examinations may not be appropriate in the dental setting, be aware of obvious physical traits that may indicate family violence (e.g., difficulty in walking or sitting, physical signs that may be consistent with the use of force, delay in seeking treatment, general neglect, financial neglect).
2. **Behavior assessment.** Judge the patient's behavior against the demeanor of patients of similar maturity in similar situations.
3. **Health histories.** If you suspect child maltreatment, it can be useful to obtain more than one history, one from the child and one separately from the adult. If you suspect intimate partner violence or elder abuse and neglect, also try to separate the patient from any suspected perpetrator to conduct the history.
4. **Orofacial examination.** Look for signs of violence, such as multiple injuries or bruises, injuries in different stages of healing, or oral signs of sexually transmitted diseases.
5. **Consultation.** If indicated, consult with the child's physician about the patient's needs or your suspicions.

Steps in Reporting Suspected Child Abuse or Neglect

1. Documentation. Carefully document any findings of suspected abuse or neglect in the patient's record.
2. Witness. Have another individual witness the examination and note and co-sign the records concerning suspected child abuse or neglect.
3. Report. Call the appropriate child protective services (CPS) or law enforcement agency in your area, consistent with state law. Make the report as soon as possible without compromising the child's dental care.
   - The telephone number for reporting is _____.
4. Necessary information. Have the following information available when you make the report:
   - name and address of the child and parents or other persons having care and custody of the child
   - child's age
   - name(s) of any siblings
   - nature of the child's condition, including any evidence of previous injuries or disabilities

- any other information that you believe might be helpful in establishing the cause of such abuse or neglect and the identity of the person believed to have caused such abuse or neglect.

Dealing with Suspected Intimate Partner Violence or Elder Abuse and Neglect

Reporting adult victims of family violence may or may not be appropriate. State laws vary considerably on mandated reporting of adult victims of family violence, and safety issues will affect your decision to intervene. Consult local authorities on reporting requirements for adults and the elderly who may be victims. Ensure that you protect both patient confidentiality and the health and safety of both the patient and your office staff.

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CLINICAL PROTOCOL 16

Oral Health Care Management for the Patient with Diabetes

Overview

The attainment of optimal oral health outcomes in patients with diabetes is determined by the level of the patient's adherence to their prescribed medical therapy (diabetes self-management) and the presence of medical complications resulting from diabetes. The role of the dental professional is to reinforce the basic principles of diabetes care, recognize medical and dental complications of this disease, and ultimately improve the patient's quality of life.

Medical History Evaluation

1. Is the patient adherent to medical recommendations for care of his or her diabetes?
   - Patients using multiple insulin injections or insulin pump should self-monitor blood glucose three or more times a day; others on less frequent injections, noninsulin therapy, or nutrition therapy should use self-monitoring as a guide to managing their blood glucose (70 to 130 mg/dL before meals; <180 mg/dL 2 hours after a meal). Note: Ideally, diabetes medications should keep blood glucose levels within these ranges (ADA, 2012). Continuous glucose monitoring is now possible. The technology involves a sensor inserted just under the skin that measures blood glucose every 5 minutes and a transmitter that picks up information from the sensor and sends it to a monitor or an insulin pump. The information is displayed in graphic form for the patient and can be sent electronically to a physician for evaluation. The technology will be useful for those having trouble controlling glucose levels to monitor exactly when high and low fluctuations are occurring and for those with hypoglycemic unawareness, among others.
   - Medications should be taken as prescribed by their physician.
   - Patients should undergo yearly updates of basic diabetes self-management education.
2. Ask questions that will help to determine the patient's level of control of their disease.
   - How are you feeling today?
   - What type of diabetes do you have and when were you diagnosed?
   - When was your last visit to your physician (diabetes) and how often do you go?
   - From which health care providers do you seek care on a regular basis?
   - What medications (prescription and over-the-counter) do you take?
   - Do you administer insulin injections by self-injection or by means of an insulin pump?
   - Are you taking the medications as they were prescribed for you?
   - Do you know your glycosylated hemoglobin (A1C) value, and when was your last A1C test done (should be <7%, normal range: 4.5 to 6.5%; obtained two to four times per year)?
   - Do you smoke or use tobacco products? If so, how much?
   - How often do you check your blood sugar and what was the most recent value?
   - Have you had any problems with low or high blood sugar levels recently?
   - Have you had any heart or vascular problems?
   - When did you last have a dilated eye exam? (yearly)
   - Do you have pain or cramps in your legs at any time?
   - Do you have any open sores, numbness, pain, tingling, or coldness in your feet? If so, how often and where?
   - Do you have any trouble swallowing?
   - If you take insulin injections, where do you administer them? (important to rotate sites)
3. Emphasize that proper diabetes management leads to better oral health, which will positively impact the patient's overall health.
4. After obtaining or updating the medical history, determine whether there are medical issues that warrant immediate care prior to elective dental procedures being performed.
   - Blood pressure <130/80 mm Hg
5. Medical referral is appropriate if there are serious issues related to the patient's diabetes care, self-care regimen, or if the patient presents with problems not previously noted or diagnosed.

Oral Assessment

1. **Salivary glands**
   - Look for swellings in glands
   - Assess salivary flow and quality of saliva

2. **Periodontal examination**
   - Gingival assessment for bleeding and clinical signs of disease
   - Full mouth probing on initial examination and annually thereafter
3. **Examine all tooth surfaces**
   - Caries
   - Erosions
   - Abfractions
   - Other abnormalities
4. **Examine soft tissues for pathology**
5. **Evaluate the patient's hands for problems that would interfere with dental self-care regimens**

Dental Treatment Modifications

The decision to obtain a medical consultation, postpone treatment, or modify treatment should be based on the patients' level of disease control, as evidenced by their answers to the questions above. The goal in cases where consultation, postponement, or modifications are indicated is to improve the patient's glycemic control and minimize the risk of an emergency during dental procedures. If patients have good control of their disease, no modifications are necessary during routine dental treatment. In all instances, balance treatment needs with patients' medical status and their motivation and ability to follow dental self-care recommendations *without* limitations.

The following are examples of modifications that may be indicated for scaling and root planing or other invasive dental procedures including oral and periodontal surgery:

- Schedule patients for morning appointments after they have taken their medications and have eaten.
- Prepare patients in advance for dietary changes that may be associated with dental procedures that have the potential to affect their ability to eat. Diabetes educators or dietitians can recommend various diets that will conform to posttreatment requirements and provide proper nutrition for the patient.
- Consider antibiotic prophylaxis if the patient's blood glucose level exceeds 200 mg/dL (use American Heart Association [AHA] recommendations or consult with the physician).
- Do not attempt to adjust insulin doses for routine dental treatment. Any adjustment to insulin doses should be done only after consultation with the patient's physician and/or core diabetes team member.

Diabetes Resources for Dental Professionals

- National Institute of Diabetes, Digestive, and Kidney Disorders: *www.niddk.gov*
- Centers for Disease Control and Prevention, Division of Diabetes Translation: *www.cdc.gov/diabetes*
- National Diabetes Education Program: *www.ndep.nih.gov*
- Working Together to Manage Diabetes: A Guide for Pharmacists, Podiatrists, Optometrists, and Dental Professionals (patient education materials, health care professional materials): *http://www.ndep.nih.gov/publications/PublicationDetail.aspx?PubId=26.*

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CLINICAL PROTOCOL 17

Oral Health Care Management for the Patient with Heart Disease

Cardiovascular disease continues to be the leading cause of death in the United States, although a greatly increased number of individuals are living relatively normal lives despite the presence of one or more manifestations of this condition. It is beyond the scope of this section to fully address the nature of various heart conditions and principles of dental management of patients with the conditions. The reader should review one of several oral medicine texts that discuss cardiovascular diseases and their management in detail. However, we attempt to outline certain general principles that apply to dental management of individuals with various forms of this disease.

Valvular Heart Disease/Heart Murmur

1. Heart damage from conditions such as rheumatic heart disease, congenital heart defects, systemic lupus erythematosus, mitral valve prolapse, and others may place individuals at increased risk of developing infectious endocarditis (IE), a life-threatening infection. However, there is minimal evidence associating bacteremias produced during dental treatment with episodes of IE to a greater extent than that associated with bacteremias induced by normal oral functions such as chewing, toothbrushing, and flossing. Consequently, the AHA has recently (2007) updated their recommendations regarding dental considerations in patients at risk for IE. Prophylactic antibiotic coverage is recommended for individuals with valvular heart disease only if they have a history of IE or if they have a prosthetic cardiac valve.
2. For patients at risk (those with a history of IE or who have a prosthetic cardiac valve), some authorities believe that IE sometimes may occur following dental treatment. Consequently, certain steps are appropriate in dental management of these individuals.
3. Prophylactic antibiotic coverage is recommended for at-risk patients for all dental treatment procedures that involve manipulation of gingival tissue or the periapical region of teeth or perforation of oral mucosa. According to these recommendations, only a few specific dental procedures do not require prophylaxis. These include routine anesthetic injections through noninfected tissue,

taking dental radiographs, placement of removable prosthodontic or orthodontic appliances, adjustment of orthodontic appliances, placement of orthodontic brackets, shedding of deciduous teeth, and bleeding from trauma to the lips or oral mucosa. Use the current antibiotic guidelines established by the AHA in 2007, which are very similar to previous guidelines. The AHA emphasizes that IE is best prevented by ensuring maximal periodontal and dental health through maintaining effective oral hygiene and frequent office recall intervals. NOTE: AHA Guidelines available at http://circ.ahajournals.org/content/116/15/1736.abstract. Hard copy was published in Circulation 2007. Meanwhile a single reprint is available by calling 800-242-8721 (United States only), Reprint no. 71-0407.

4. Occasionally, prophylactic antibiotic may be inadvertently omitted during a dental procedure. In this event, prophylactic antibiotics may still be effective if administered within the first 2 hours following the procedure.
5. Medical consultation may be indicated to determine the nature of the patient's risk during dental treatment. If immediate dental treatment must be administered before medical consultation, use the AHA recommendations for prophylactic antibiotic coverage during dental emergency treatment.

Congenital Heart Defects

1. Heart defects that are present at birth can affect any part or function of the heart. Today, surgical correction of these defects is often quite successful, but patients may continue to be at risk for complications during dental treatment. Consequently, medical consultation is imperative to determine the true nature of the patient's health status.
2. Prophylactic antibiotic coverage may be required if the risk of IE persists. It is recommended if cyanotic congenital heart disease, including shunts and conduits, is present for 6 months following successful repair with a prosthetic patch or device. Patients with incompletely repaired defects require antibiotic premedication, as do patients with congenital heart defects who have experienced IE or who have received a prosthetic valve at any point in their lives.
3. Be aware of the patient's drug and medical history and be alert for any signs or symptoms that may indicate the continuing presence of a heart defect.

Ischemic Heart Diseases (Coronary Artery Disease)

1. Partial blockage of heart arteries (atheroma) may impair blood supply to the heart, leading to pain on exertion (angina) or death (myocardial infarction). Patients with this condition are at risk of serious complications during dental treatment, and medical consultation is imperative prior to elective dental therapy. Practitioners must remain alert for signs or symptoms of developing ischemic heart disease during dental treatment.
2. Vasoconstrictors in local anesthetics (epinephrine or its equivalent) may be needed to obtain effective local anesthesia. However, most authorities recommend limiting total epinephrine to that contained in two to three carpules of local anesthetic with 1:100,000 epinephrine (0.02 mg per carpule) or its equivalent in individuals with ischemic heart disease. There does not appear to be any advantage in substituting levonordefrin for epinephrine, and intraosseous or intraligamental injections should be avoided. The use of vasoconstrictors on retraction cord is contraindicated.
3. An office stress-reduction protocol is essential. Dental therapy should be administered in a calm and relaxing atmosphere, and conscious sedation techniques should be considered. Profound dental anesthesia is very important, and procedures should be kept short.
4. In the event that a patient experiences an ischemic attack during dental treatment, the dental procedure should be terminated and the patient should be placed in a semisupine position; 100% oxygen should be administered and vital signs monitored. If necessary, nitroglycerin 0.2 to 0.4 mg should be administered and repeated if needed. In severe office emergencies, the Emergency Medical System (EMS) should be activated and, if necessary, external cardiac defibrillation administered by trained office personnel.

Hypertrophic Cardiomyopathy

1. Hypertrophic cardiomyopathy is a genetically derived heart enlargement that may go undetected for many years. The enlargement may impair normal heart function and, as a result, some affected individuals may experience unexpected sudden cardiac arrest, often during exercise or stressful situations. Dental patients who report a history of this condition should be referred to their physician for medical consultation to determine their health status and to ensure that dental therapy can be safely performed.
2. Patients with hypertrophic cardiomyopathy are at some risk of developing IE, but according to the recent recommendations of the AHA, prophylactic antibiotic coverage is not required for dental treatment unless the individual has a history of IE or a prosthetic heart valve. In this event, appropriate antibiotic prophylaxis should be administered in keeping with the recommendations of the AHA.
3. A dental office stress-reduction protocol should be followed as described above.
4. If a patient becomes symptomatic during dental treatment (e.g., syncope, chest pains, arrhythmia, loss of consciousness), the procedure should be terminated and the EMS activated. Nitroglycerin and other vasodilating drugs are contraindicated in these patients, but 100% oxygen and appropriate cardiopulmonary resuscitation should be performed if necessary.

Cardiac Arrhythmias

1. Abnormal heart rhythms can be induced by any condition that influences normal electrical impulses to the heart muscle. Arrhythmias may range from a slow

heartbeat (bradycardia) to a rapid beat (tachycardia), loss of atrial rhythm (atrial fibrillation), or loss of ventricular rhythm (ventricular fibrillation). Individuals who experience atrial fibrillation are at increased risk for stroke, while ventricular fibrillation can result in death. Medical consultation is required for any patient who reports a history of significant cardiac arrhythmias or who shows signs or symptoms of the condition.

2. Local anesthetics containing vasoconstrictors should be limited to two to three carpules of anesthetic containing 1:100,000 epinephrine or its equivalent. Local anesthetic should be administered slowly, and no vasoconstricting agent should be used on retraction cords.
3. Prophylactic antibiotic coverage is not required for dental treatment based solely on a history of cardiac arrhythmias. However, complications of the patient's heart condition may create an indication for its use.
4. An interoffice stress-reduction protocol should be followed as described above.
5. Cardiac pacemakers are often used today to control cardiac arrhythmias, and an increasing number of individuals with life-threatening ventricular arrhythmias are being treated by placement of automatic implanted cardioverter defibrillators (AICD). The presence of these devices does not represent a contraindication to dental treatment, nor does it require prophylactic antibiotic coverage. However, older AICDs (more than 10 years old) sometimes may be disrupted by electromagnetic currents and caution should be taken with the use of electrosurgical devices and magnetorestrictive ultrasonic instruments.
6. AICD patients will receive an electrical shock if their device is activated. Consequently, the patient's experience with the device should be discussed in advance. Most devices are not activated for several seconds after the beginning of the arrhythmia, and patients should be asked to forewarn the dental staff if they perceive a possible pending electrical shock. The treatment procedure should be suspended and all dental items removed, when possible, before the shock. A mouth prop should be considered for use with these patients to minimize the risk of injury to them or the dental practitioner. Under most circumstances, the patient will return to normal rhythm after the shock. If this does not occur, the EMS should be activated and cardiopulmonary resuscitation initiated if needed.

Congestive Heart Failure

1. Congestive heart failure occurs when a weakened heart muscle is no longer able to pump adequate quantities of oxygenated blood to the body. It may be caused by any of the conditions discussed above, and it results in fluid accumulation in the lungs along with kidney failure. Consequently, affected individuals may experience shortness of breath, peripheral edema, angina, cyanosis, and chronic fatigue. Despite the serious life-threatening nature of the condition, current cardiology treatment modalities may significantly prolong life. Many individuals with congestive heart failure can be expected to seek dental care when needed.
2. Medical consultation is imperative to determine a patient's overall health status. Patients with severe congestive heart failure are not candidates for routine dental care, but many others are. Antibiotic prophylaxis may be indicated depending on the etiologic factors associated with heart failure. When antibiotics are indicated, the recommendations of the AHA can be followed.
3. Medications used in the treatment of heart failure sometimes may induce gingival overgrowth or a spontaneous dry cough that may interfere with routine dental treatment.
4. Stress-reduction protocols are indicated for dental treatment, as described above.
5. The dental practitioner must remain alert for signs or symptoms of cardiac crisis, and must be prepared to activate the EMS and administer cardiopulmonary resuscitation if needed. Prophylactic antibiotic coverage is not required for dental treatment unless the patient has a history of IE, a prosthetic heart valve, or prophylaxis is requested by the physician.

The Surgically Corrected Heart

1. Surgical correction of congenital heart defects, valvular stenosis, or occluded coronary arteries has become a standard of care in cardiology, and heart transplantation is an acceptable treatment option. Medical consultation is important to determine the cardiac treatment outcomes for dental patients who report such surgical procedures. Prophylactic antibiotic therapy is not required for dental treatment in patients who have had successful heart surgery such as correction of minor congenital defects and coronary artery bypass grafts. However, patients with artificial heart valves or partially repaired congenital defects will require antibiotic prophylaxis using AHA guidelines.
2. It is important to be aware that severe periodontal disease may predispose patients to recurrence of their original heart condition such as coronary artery occlusion or stroke.

Coronary Artery Stents

1. Placement of coronary artery stents has become increasingly common in the management of individuals with coronary artery disease. Individuals receiving these stents may remain on anticoagulant medication for life. Consequently, medical consultation may be necessary to determine any necessary dental treatment precautions.
2. Antibiotic prophylaxis is not required based solely on the presence of coronary artery stents following a 4- to 6-week healing period. In most instances, no reduction in anticoagulant therapy is required for routine dental procedures, including periodontal surgery and extractions.

Heart Transplantation

1. Heart transplants are currently being used to manage a variety of cardiovascular conditions. Improvements in protocols to insure good donor-patient tissue matches, improved surgical techniques, and the use of immunosuppressant drugs to prevent organ rejection have markedly increased the success rate. However, transplants are not without complications, and medical consultation is essential before performing dental therapy. Ongoing close medical-dental coordination is important to ensure that the dentist is aware of any developing condition that may adversely affect rendering safe and effective dental care.
2. Gingival enlargement may occur as a side effect of antirejection drugs such as cyclosporine, and immunosuppressant drugs may cause an individual to be more susceptible to opportunistic oral infections, osteoporosis, or avascular osteonecrosis.
3. In general, prophylactic antibiotic coverage is not required for dental treatment after a normal healing period of up to 6 months. However, the AHA recommends antibiotic prophylaxis for heart transplant recipients if they develop cardiac valvulopathy. Organ recipients who do not achieve maximal cardiac function or who require extensive immunosuppressive therapy may remain at risk of life-threatening infections. Consequently, consultation with the patient's physician is recommended. In most cases, the antibiotic guidelines recommended by the AHA probably would be appropriate unless more stringent antibiotic coverage is requested by the cardiologist.
4. Optimal periodontal and dental health is extremely important for transplant recipients. It should be noted that immunosuppressive medications may mask the usual signs and symptoms of oral infections, so very careful dental/periodontal examination is indicated. Meticulous oral hygiene measures and frequent maintenance recall visits help to insure prevention or early detection of developing dental or periodontal problems.
5. Due to loss of innervation to transplanted hearts, patients may experience "silent" painless myocardial infarction, so close monitoring of vital signs in imperative.

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CLINICAL PROTOCOL 18

Supplements for Oral/Systemic Health

Herbal Supplements and Dental Care

During the last two decades, use of herbal supplements in the United States has steadily increased, with approximately 22% of adults reporting recent usage. More frequent use of herbal products is reported among elderly and medically compromised individuals. Many consumers are unaware of the potential adverse effects from these products and about 70% of them do not even disclose their use to health care providers.

Being classified as dietary supplements within the realm of complementary and alternative medicine, herbal supplements are not regulated by the Food and Drug Administration (FDA). Herbal supplements can be associated with possible adverse effects and interactions with a number of prescription and over-the-counter medications. The lack of regulatory restrictions, escalating utilization of the products, and the low rate of reporting by consumers has raised concerns in the medical community regarding the safety and efficacy of herbal supplements. As a result, there has been increased interest in the last several years to address these concerns within medical settings.

It is documented that about two dozen types of herbs are variably used by consumers, either singly or in combination with other items. Of these, close to one-half appear to have greater dental significance relative to the rest. These products are listed in the accompanying table along with their most relevant bioactive constituents and potential clinical implications.

Herbal Supplements and Their Most Relevant Bioactive Constituents and Potential Clinical Implications

Herbal supplements	Relevant bioactive constituents	Potential clinical implications
Feverfew	Parthenolide	Antiplatelet with enhanced risk of bleeding
Garlic	Ajoene, alliin, allicin	Antiplatelet with enhanced risk of bleeding
Ginkgo biloba	Ginkgolide	Antiplatelet with enhanced risk of bleeding
Ginseng	Ginsenosides	Antiplatelet with enhanced risk of bleeding; immunostimulant with antagonistic effect on immunosuppressing drugs
Green tea	Catechins	Antiplatelet with enhanced risk of bleeding
Echinacea	Alkamides	Immunostimulant with antagonistic effect on immunosuppressing drugs
Kava	Kava lactones, kava pyrones	Central nervous system (CNS) depressant potentiating effects of sedatives
St. John's wort	Hypericin, hyperforin	Monoamine oxidase (MAO) and catecholamine neuronal reuptake inhibitor with possibility of causing serotonergic syndrome with certain opioid agonists; potentiating effects of sedatives
Valerian	Sesquiterpenes	CNS depressant potentiating effects of sedatives

Therefore, use of green tea, garlic, ginkgo biloba, feverfew and ginseng can potentially cause bleeding problems in dental practice after major oral and maxillofacial surgery. These herbs can also increase the hemorrhage potential in patients who are taking medications such as warfarin, aspirin, ibuprofen and other platelet aggregation inhibitors. Ginseng and echinacea also induce immune-stimulating effects antagonistic to immunosuppressant drugs, including corticosteroids. Centrally-acting herbal products such as kava, St John's wort, and valerian can augment sedation when taken in combination with CNS-depressing medications like benzodiazepines, opioid analgesics, and nitrous oxide. St John's wort also has the potential to produce serotonergic syndrome (slight to life-threatening increases in heart rate, blood pressure and temperature among others) when combined with certain opioid agonists including meperidine and tramadol.

It is expected that the adverse effects and drug interactions of herbal supplements are more likely to occur when the products containing the expected active ingredients are taken at high doses and/or for prolonged duration. However, since all products identified as a particular herb may not contain equal quantities of active ingredient(s) due to the lack of strict manufacturing and/or quality control requirements, the situation becomes complicated for accurate predictions of effects.

Clinical Guidelines

Dental health caregivers should be aware of herbal usage and their potential effects in dental patients. It is recommended that dental care providers routinely ask patients about herbal use as part of routine evaluation. However, under present circumstances, it is hard to establish meaningful correlations between herbal products and the effects they could produce. Until standardization and stricter regulation of products is realized, the clinical assessment of the effects of herbal products will remain an empirical undertaking performed on an individual basis.

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Adapted from Abebe W, Herman W, Konzelman J. Herbal supplement use among adult dental patients in a US dental school clinic: prevalence, patient demographics and clinical implications. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;111:3210–3325.

CLINICAL PROTOCOL 19

Oral Health Care Management for the Patient with Cancer

When a patient presents with cancer, dentists and dental hygienists have an important role in performing the pretreatment oral evaluation, providing oral health care during cancer therapy, and providing posttreatment oral care management, including long-term treatment planning.

Prevention and management of oral complications can have a significant impact on the overall health of these patients and their quality of life. Such complications may include painful mucositis; bacterial, candidal, and viral infections; xerostomia; thickened oral secretions; salivary gland hypofunction; trismus and muscle dysfunction; radiation caries; teeth sensitivity; bleeding in the oral cavity and gingiva; difficulty eating and swallowing; and/or osteoradionecrosis of the jaws.

Pretreatment Oral Evaluation and Oral Care Guidelines

Pretreatment oral evaluation is recommended for patients with cancer prior to the initiation of cancer therapy. The following protocol should be followed:

- Consult with the oncology team to gain information about the cancer treatment plan.
- Perform a thorough medical history evaluation; head and neck examination, including an extra- and intraoral examination; and radiographic, restorative, and periodontal examinations, and review baseline blood laboratory findings.
  - Intraoral edentulous regions must be examined for impacted teeth, retained root tips, and osseous disease that may worsen during cancer therapy.
- Record baseline data of the oral cavity for comparison and monitoring of sequela from the effects of radiation therapy and/or chemotherapy.
- Assess the degree of oral disease(s) that may or may not exacerbate during or after cancer therapy.
- Provide education to patients about the importance of oral hygiene and the importance of adhering to individualized oral care management strategies for before, during, and after cancer therapy.
  - Provide instruction on proper tooth brushing (a soft, nylon bristled toothbrush is required) and use of interdental aids.
  - Fabricate custom fluoride trays of a soft flexible mouthguard material for use during and after cancer treatment.
  - Provide counseling about treatment for sensitivity to flavoring agents and spicy foods **(refer to Clinical Protocol #6)**.
  - Recommend the patient seek the services of a registered dietician for nutritional counseling.
  - For edentulous patients, advise on the protocol for removing prosthetic appliances.
  - Provide nutritional counseling specifically targeting a noncariogenic nonfermentable carbohydrate diet.
  - Provide strategies that address xerostomia (**refer to Clinical Protocol #4**).
  - Encourage the patient to drink water.
  - Inform the patient about the potential risks from radiation caries and/or osteoradionecrosis, when applicable.
- Perform preventive prophylaxis or therapeutic debridement appointments.

- When head and neck radiation and chemotherapy are scheduled, the following recommendations should be considered:
  - Nonrestorable teeth with a poor or hopeless prognosis, teeth with acute infection, and/or teeth with severe periodontal disease that may predispose the patient to radiation- or chemotherapy-induced complications (i.e., osteoradionecrosis, radiation caries, sepsis) should be extracted.
  - Chronic inflammatory lesions in the oral cavity and the jaws, including sources of infection, should be treated.
  - Symptomatic nonvital teeth should be endodontically treated 1 week prior to cancer therapy; treatment of asymptomatic nonvital teeth even with periapical pathology can be delayed or postponed until after cancer therapy.
- Teeth extraction and surgical guidelines:
  - Perform extractions at least 2 to 3 weeks prior to cancer therapy.
  - Allow adequate time for wound healing and ensure primary closure during healing.
  - Avoid hemostatic packing agents in bone that can serve as a nidus for potential infection.
  - Provide a blood transfusion when the platelet count is less than 50,000/mm^3.
  - Delay procedure when the white blood cell count is less than 2,000/mm^3; or the neutrophil count is less than 1,000/mm^3.
  - Prescribe antibiotic prophylaxis, when indicated.

Oral Care during Cancer Therapy

It is advised that patients who undergo cancer therapy receive dental treatment at appropriate times between cancer therapy cycles. The following guidelines and strategies are outlined for patients who develop oral complications during and after head and neck cancer therapy.

- Provide routine dental care/invasive oral procedures
  - Consult with the oncologist for medical clearance to treat.
  - Perform dental procedures approximately 2 to 3 weeks after chemotherapy or when the patient feels immune competent/healthier.
  - The following laboratory guidelines are referenced below when dental treatment is planned:
    - WBC count is greater than 2,000 cells/mm^3
    - neutrophil count less than 1,000/μL or in patients with chronic indwelling venous access catheters (The 2007 American Heart Association antibiotic prophylaxis guidelines for infective endocarditis is empirically recommended.)
    - platelet count is greater than 50,000 cells/mm^3
- Management of complications of radiation therapy and chemotherapy:
  - Nutritional intake
    - Consult with the registered dietician or with other professionals on the oncology team to monitor weight and nutritional intake.
  - Mucositis:
    - **Refer to Clinical Protocol #13**, and consider the following:
    - Advise the patient to avoid tobacco, alcohol, and carbonated drinks.
    - Advise the patient to follow a soft diet and drink water.
    - Advise the patient to use a humidifier.
    - Treat superimposed or secondary oral infection.
    - It is recommended to use benzydamine for prevention of radiation-induced mucositis in patients with head and neck cancer receiving moderate-dose radiation therapy.
    - It is not recommended to use chlorhexidine gluconate to treat oral mucositis.
    - It is not recommended to use sucralfate or antimicrobial lozenges for the prevention of radiation-induced oral mucositis.
  - Xerostomia
    - Refer to **Clinical Protocol #4**
  - Radiation caries
    - Advise the patient to use custom fluoride trays with a 0.5% neutral sodium fluoride gel or use a brush-on application of 5,000 ppm fluoride (e.g., Prevident).
    - It is advised to restore early carious lesions.
    - Encourage the patient to have recall appointments every 2 to 3 months.
  - Teeth sensitivity
    - Advise the patient to use topical neutral sodium fluoride, or have professional applications of fluoride varnish.
  - Loss of taste
    - Advise the patient to use zinc supplementation.
  - Osteoradionecrosis
    - When considering dental surgery, caution must be employed.
    - Monitor the need for hyperbaric oxygen therapy.
  - Trismus or facial muscular dysfunction
    - Advise the patient to use tongue blades of various thickness. Insert tongue blades between the upper and lower dentitions/edentulous ridges to ensure opening and closing of the jaws.
  - Mouth or gingival bleeding
    - When the platelet count falls below 50,000, platelet transfusion may be required.
    - When the platelet count is less than 50,000/mm^3, it is recommended patients use toothettes (sponge applicators), a washcloth, or gauze moistened with warm water or an antimicrobial solution to clean their teeth/edentulous ridges.
    - Hemostatic agents to help control bleeding or agents to counteract clot breakdown are recommended; or refer the patient to the oncologist for further evaluation.

Oral Care Post Cancer Therapy

In general, long-term oral complications associated with cancer and its therapy include chronic xerostomia, loss of

taste, bone alterations, muscle and temporomandibular joint dysfunction, and/or other related problems. The following guidelines are outlined for patients after head and neck cancer therapy.

- Consider utilizing oral care instructions described in the sections above.
- Consult with the oncologist for medical clearance to treat.
- Advise patient to maintain 1- to 3-month recall appointments during the first 2 years to monitor oral complications and to examine for possible latent metastases; maintain 3- to 6-month recall appointments thereafter.
- Ensure optimal oral hygiene.
- Advise patient to continue with application of fluoride.
- Complete dental procedures that fit the patient's needs under optimal systemic health conditions.

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CLINICAL PROTOCOL 20

Oral Health Care Management for the Patient with HIV/AIDS

Recognition and diagnosis of oral manifestations associated with HIV/AIDS may be the first indication of suspected HIV virus. In general, factors that increase the probability of developing such lesions are caused by a CD4 T lymphocyte cell count less than 200 cells/mm^3 and a viral load greater than 3,000.

Dental Treatment Planning and Considerations

Due to the multiple systemic effects of HIV infection and the evolving nature of the disease, the patient's medical history and laboratory outcomes must be updated prior to dental treatment in order to assess CD4/8 T cell lymphocyte count, white blood cell count, viral load, platelet count, and hemoglobin levels. The CD4+ T lymphocyte count and WBC count indicate the level of immunosuppression; platelet count indicates potential bleeding tendencies; and viral load indicates susceptibility to opportunistic infections and the rate of progression of the AIDS virus. Thus, it is prudent to consult with the medical provider prior to any dental treatment.

Antibiotic Prophylaxis to Prevent Infective Endocarditis

When indicated, prophylactic antibiotics to prevent infective endocarditis should be prescribed according to the 2007 American Heart Association Guidelines.

Antibiotic Coverage and the HIV-Infected Patient

When the CD4+ T lymphocyte count is less than 200 cells/mm^3 or when the neutrophil count drops below 500 cells/mm^3 (neutropenia), antibiotic prophylaxis is recommended to prevent opportunistic infection. Patients at this advanced stage of the disease may already be taking antibiotics to prevent opportunistic infection; therefore, additional antibiotics may not always be required.

Bleeding Abnormalities

For patients with a history of, or indications for, increased bleeding tendencies, periodontal and surgical procedures should be approached conservatively. The following laboratory guidelines should be considered:

- When performing invasive dental treatment, platelet counts should be greater than 60,000 platelets/mm^3.
- Prothrombin time (PT)/partial thromboplastin time (PPT) laboratory values should be no more than twice their normal values.
- Platelet count of 50,000/mm^3 or greater may demonstrate postoperative bleeding complications; thus, attention to hemostatic measures is recommended.
- Easy bruising and bleeding secondary to surgery are encountered when levels fall below 60,000 platelets/mm^3.
- Severe thrombocytopenia (<50,000 platelets/mm^3) may require platelet replacement prior to surgical or scaling and curettage procedures.
- When platelet levels fall below 20,000 platelets/mm^3, spontaneous bruising, petechiae, and GI bleeding are likely to occur.
- When planning for invasive dental procedures, any indicated screening laboratory blood tests are usually conducted shortly before (i.e., 1 to 2 days) performing procedures.

Anemia

- Periodontal and minor surgical procedures (e.g., single extraction) are usually considered routine for patients with a hemoglobin level above 7 g/dL and no bleeding abnormalities.
- When invasive dental procedures are likely to cause profuse bleeding, approach procedures conservatively when hemoglobin levels fall below 7 g/dL.

Local Anesthesia

- Inferior alveolar block injections can result in medical complications in patients with a recent history of, or indications for, increased bleeding tendencies; thus, it is recommended that local infiltrations or intraligamentary injections be used.

Oral Lesions Commonly Associated with HIV/AIDS

Oral Conditions and Lesions	Oral Complications and Treatment Considerations
1. Lymphadenopathy	Nodes tend to be larger than 1 cm in diameter, with multiple sites and persistent enlargement.
2. Oral candidiasis	Pseudomembranous, erythematous, angular cheilitis, and hyperplastic candidiasis are the most common intraoral manifestations of HIV infection. Refer to Clinical Protocol #1 and #5 for diagnostic tools and supplies and for treatment.
3. HIV-associated periodontal disease	Linear gingival erythema, necrotizing ulcerative gingivitis, and necrotizing ulcerative periodontitis generally do not respond to improved plaque control and conventional periodontal therapy. Treatment should include oral hygiene instructions, periodontal debridement and surgical debridement, use of topical chemotherapeutic agents and povidone-iodine, and pain control and management of infection. Regular and frequent supportive periodontal care is highly recommended.
4. Herpes simplex virus	Lesions are more widespread, occur in an atypical pattern, and may last for months. Refer to Clinical Protocol #8 for palliative treatment.
5. Varicella-zoster virus (VZV)	VZV is more common and more severe in the HIV-infected patient. Intraoral manifestations are often severe and can lead to bone involvement with loss of teeth.
6. Oral hairy leukoplakia (OHL)	OHL is generally found on lateral borders of the tongue, and is associated with Epstein-Barr virus infection.
7. Neoplastic lesions	Human herpes virus type 8 appears to be involved in Kaposi sarcoma (KS) development. KS in the infected HIV patient is diagnostic of AIDS. Medical management includes radiation/chemotherapy; dental treatment may include: laser excision, cryotherapy, or intralesional injections with vinblastine. Non-Hodgkin lymphoma in the mouth is confirmed through biopsy and histologic evaluation. Therapy includes radiation or chemotherapy.
8. Salivary gland disease	Enlargement of the salivary glands may be related to infection, cyst formation, malignancy, and xerostomia. Fine needle biopsy and radiographic imaging of the glands may be indicated to diagnose the condition. Refer to Clinical Protocol #4 for treatment considerations.

Table adapted from Little J, Falace D, Miller C, et al. *Dental management of the medically compromised patient.* 7th ed. St. Louis: Mosby Elsevier, 2008:297.

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CLINICAL PROTOCOL 21

Oral Health Care Management for the Patient Taking Anticoagulant Medications

Synopsis

Outpatient anticoagulant therapy is used today in management of individuals known to be at risk for or afflicted with various cardiovascular conditions (deep vein thrombosis, intravascular clotting, protein S or protein C deficiency, pulmonary embolism, carotid artery stenosis, atrial fibrillation, ischemic heart disease, post-myocardial infarction, prosthetic heart valves, cerebrovascular accidents, coronary stents, and other flow disturbances). There are two major types of antithrombotic drugs: anticoagulants and antiplatelet medications.

- Coumadin (warfarin sodium) is the most commonly used outpatient anticoagulant drug. It inhibits vitamin K production leading to depletion of various clotting factors. It is monitored by the PT using an International Normalized Ratio (INR). Coumadin is metabolized in the liver by cytochrome enzyme P450 as are many other drugs. Consequently, numerous drugs used in dentistry (antibiotics, aspirin, acetaminophen, nonsteroidal anti-inflammatory agents, antifungals, antihistamines, diazepam, and others) and numerous herbal agents (St John's wort, coenzyme Q10, Dong quai, feverfew, garlic, ginger, ginkgo biloba, ginsing, and others) may adversely interact with Coumadin, interfering with its anticoagulant properties. Dietary factors (malnutrition, vitamin E, reduced or increased vitamin K, mango, kiwi, and others) may influence anticoagulation as can certain systemic factors (diarrhea, malignancy, liver disease, kidney disease, systemic lupus erythematosus, and others).

  Normal INR is valued at 1.0. For Coumadin, an INR range of 2.0 to 3.0 is recommended for most anticoagulation regimens while an INR of 2.5 to 3.5 may be indicated for individuals with mechanical heart valve or those with a history of recurrent embolisms. On occasion, higher INR levels are necessary in individuals with severe cardiovascular disease.

- Antiplatelet drugs include aspirin (acetylsalicylic acid), clopidogrel (Plavix), Ticlopidine (Ticlid), and dipyridamole (Persantine). These drugs interfere with platelet aggregation or function. They are used on an outpatient

basis to prevent or control the disorders enumerated above. The drugs may be used alone or in combination (i.e., aspirin and Plavix). Antiplatelet drugs are not strongly associated with excessive bleeding following invasive dental procedures unless the drugs are used in combination with other "blood thinners." The effect of these drugs is not measured by the INR.

Anticoagulants and Dental Care

Patients who take antithrombotic drugs are at risk for excessive hemorrhage during or following invasive dental procedures. Conversely, reducing or eliminating antithrombotic therapy in association with dental appointments *may significantly increase* the risk of life-threatening cardiovascular emergencies. Consequently, the dental practitioner must weigh the risk for excessive hemorrhage against the morbidity or mortality that might be associated with discontinuing the antithrombotic therapy. Although the risk of bleeding is unwelcome, the potential severity of complications associated with temporarily stopping anticoagulant therapy appears to take precedence. Currently, most authorities recommend that anticoagulant therapy not be discontinued for minor oral surgical or periodontal treatment procedures, including scaling and root planing.

Preventing Treatment Problems in Patients Taking Antithrombotics

Anticoagulants: There are few well-controlled studies regarding anticoagulant protocols. Consequently, recommendations are primarily based on consensus expert opinion. For the sake of this discussion, we assume that the INR range is 2.0 to 3.5.

Most recent evidence indicates that therapeutic INR target levels rarely require modification to safely perform invasive oral surgical or periodontal treatment procedures. Ideally, INR should be monitored by the patient's physician on the day before or the day of surgery. During treatment, patients should be carefully monitored for signs or symptoms of cardiovascular complications, and bleeding should be managed using local measures.

Antiplatelet drugs: There is rarely a need to discontinue low-dose aspirin (81 to 325 mg) or other antiplatelet drugs for most oral surgical or periodontal procedures. On occasion, patients use both aspirin and clopidogrel simultaneously. In this event, some authorities suggest stopping one or the other medication but not both.

Dental Management Recommendations

1. Obtain a thorough medical history and evaluate morbidity of any concurrent systemic illnesses.
2. Evaluate all medications being taken, including over-the-counter, and consider the possibility of adverse drug interactions with medications you might prescribe such as antibiotics and/or analgesics. Acetaminophen in low doses or narcotics are recommended for pain.
3. Obtain medical consultation.
4. Keep procedures small and of short duration.
5. Monitor vital signs—**DO NOT TREAT IN PRESENCE OF UNCONTROLLED HYPERTENSION.**
6. **Use local measures to control hemostasis,** such as primary wound closure, direct pressure, foamed gelatin, synthetic collagen, tranexamic acid, or epsilon-aminocaproic acid (EACA) mouth rinse. If prolonged bleeding occurs, consider administration of vitamin K or, in urgent cases, fresh frozen platelets or plasma.
7. Ensure the patient is aware that compliance with management recommendations is essential.
8. Forewarn the patient of the increased risk of intraoperative and postoperative bleeding and intraoral/extraoral hematoma.
9. Avoid regional block anesthesia if possible.
10. Be alert for signs or symptoms of developing cardiovascular or other office emergencies and be prepared to activate the medical emergency system.

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CLINICAL PROTOCOL 22

Oral Health Care Management for the Patient with Renal Disease

Synopsis

The kidneys are vital organs involved in regulating body homeostasis. By the blood filtration process, they function to regulate acid-base and fluid electrolyte balance of the body. The filtration process also excretes metabolic waste products, including many drugs and foreign chemicals. Additionally, the kidneys secrete endocrines such as renin and erythropoietin, thereby playing a vital role in maintenance of blood pressure, calcium metabolism, and synthesis of red blood cells.

Diseases of the kidney are myriad. They may be hereditary in origin or they may occur secondary to other systemic diseases or disorders such as diabetes mellitus or hypertension.

Acute renal failure may result from chronic renal diseases but also may occur due to hemorrhage, severe hypotension, advanced heart failure, liver disease, obstructive biliary cirrhosis, or ischemia occurring as a complication of surgery. Acute failure may sometimes be reversible with treatment but hemodialysis may be required, especially if the condition progresses to end-stage renal disease (ESRD).

Chronic renal failure is a bilateral, progressive deterioration of functioning nephrons. It may progress insidiously but can profoundly alter the function of virtually every body organ system. The **uremic syndrome** occurs secondary to progressive renal failure due to accumulation of blood urea nitrogen (BUN), creatinine, and other metabolic waste products, ultimately leading to ESRD. The condition features azotemia (the buildup of nitrogenous waste products in the blood), impaired ability to concentrate

urine, polyuria, altered calcium/phosphorus ratios, and metabolic acidosis. It may be accompanied by numerous other systemic disorders such as hypertension, congestive heart failure, coronary artery disease, neuropathies, severe anemia, and bleeding disorders. GI disorders occur such as anorexia, nausea and vomiting, and an odor (ureic fetor) may emanate from the oral cavity due to the breakdown of the urea in saliva to ammonia.

Oral features of ESRD are numerous. Patients may experience:

1. An increase in salivary calculus formation.
2. Uremic stomatitis, which may occur in two forms. The erythemopultaceous type features dry, burning, erythematous, and painful oral tissues that may be covered with a thick gray exudate. The ulcerative form is characterized by multiple mucosal ulcerations.
3. Xerostomia is a nearly universal complaint.
4. Gingival hemorrhage and hematoma formation may occur after slight trauma.
5. Enamel hypoplasia and brownish discoloration of the teeth occurs in children, and dental pulps may appear narrowed.
6. Bacterial, viral, or fungal oral infections are common.
7. Increased esophageal reflux may cause dental erosion and oral discomfort.
8. Secondary hyperparathyroidism may induce fine granular metastatic calcifications in the oral connective tissue and radiographic evidence of hyperparathyroidism may include loss of lamina dura in the alveolar bone around the teeth. Osteopenia or osteoporosis may result from renal failure, creating a "ground glass" radiographic appearance to the jaw bones. Extraction sockets may retain their lamina dura for years and sclerotic radiopacities of bone have been reported. Small unilocular or multilocular cystic jaw lesions may represent pseudocysts or giant cell tumors (the brown tumor of hyperparathyroidism). Increased mobility of teeth may be present in the absence of periodontal pockets.
9. Periodontal inflammation may be more severe than for normal plaque-induced gingivitis.

Treatment of End Stage Renal Disease

ESRD is treated with hemodialysis in which nitrogenous and other toxic metabolic products are periodically removed from the blood. This is usually accomplished by exchange between the patient's plasma and a dialysate liquid through a semipermeable membrane that allows toxins to diffuse out while retaining formed elements and proteins in the blood. Although this technique is not equivalent to normal renal function, it does sustain life. Typically dialysis patients undergo this treatment three times weekly with each session lasting 3 to 4 hours. During these treatments and afterward, patients receive anticoagulant therapy, usually heparin, which loses its blood thinning effect quickly after treatment.

To gain access for hemodialysis, it is necessary to create a shunt or an arteriovenous fistula from artery to vein, usually in the forearm. Peritoneal dialysis is accomplished by placement of a catheter through the abdominal wall into the peritoneum and insertion of a dialysate that is removed after the fluid exchange of toxic substances. Unfortunately, this technique requires treatment virtually every day or a continuous cyclic dialysis that exchanges dialysate every 6 to 8 hours daily. Peritoneal dialysis does not require heparinization and allows more personal freedom for the patient.

The ultimate treatment for ESRD is organ transplantation. Although the success rate is high, individuals receiving organ transplants are at risk for organ rejection and consequently must take immunosuppressant drugs (cyclosporine, azathiprine, mycophenolate mofetil (CellCept), or others) for life. This immunosuppression may result in an increased risk for bacterial, viral, or fungal infections while the medications used may result in drug-induced liver disease. It should also be noted that individuals who have received hemodialysis are at very high risk of having contracted viral hepatitis. There is also a markedly greater risk for developing skin or mucosal malignancies in individuals taking antirejection drugs.

Dental Management Considerations

1. **Medical consultation.** Close medical/dental coordination is essential in management of individuals with severe renal disease; those receiving renal dialysis, or transplant recipients. When possible, the dentist should be involved in the treatment planning stage prior to initiation of dialysis or organ transplantation. The dentist should ask for information regarding the patient's overall health status and ability to withstand the proposed dental treatment.
2. **Antibiotic prophylaxis**. Antibiotic prophylaxis may be indicated for individuals with diminishing renal function or with acute or chronic renal failure. Individuals with renal failure should not receive routine dental treatment. However, if emergency extractions or other procedures are required, antibiotic prophylaxis should be administered using the guidelines established by the AHA for prevention of infective endocarditis. However, individuals with known infections by specific microorganisms should be administered antibiotics most likely to be bacteriocidal for those organisms.
3. **Potential problems with dental care**:
   a. Patients with renal failure are not candidates for dental therapy other than for emergency treatment such as extractions, or management of abscess formation. Renal dialysis patients may receive limited dental treatment with medical consent. If surgery is required, delayed wound healing should be expected and any therapy likely to induce a bacteremia places patients at risk for serious, potentially life-threatening complications. Several drugs used in dentistry (acyclovir, aminoglycosides, tetracyclines, sulfonamides, and polypeptide antibiotics [bacitracin and polymyxin]) are potentially nephrotoxic and potassium penicillin may increase serum potassium levels.

b. Oral infections can be life threatening, yet immunosuppressive medications taken by renal transplant patients may mask the usual signs and symptoms of infection and inflammation to include those associated with periodontal diseases. Patients receiving hemodialysis are highly susceptible to bacterial, viral, or fungal infections. Invasive dental treatment procedures are likely to induce bacteremia, but this effect can be minimized if the treatment is timed to be performed shortly after a dialysis session when the patient's resistance is improved.
c. Excessive hemorrhage may occur following dental treatment due to the use of heparin in conjunction with dialysis. It should be noted that IE may occur in renal transplant patients who do not have a history of valvular damage.

4. **Dental treatment considerations.** No firm protocols have been established for dental management of patients with chronic renal disease or ESRD or for recipients of renal transplants.
a. Whenever possible, the dentist should participate in treatment planning for patients scheduled to initiate hemodialysis or to receive renal transplants. If the patient's medical status allows, hopeless and questionable teeth should be extracted before the renal treatment begins and all oral foci of infection eliminated or controlled. Effective oral hygiene measures should be taught and antibiotic mouth rinses, such as those containing chlorhexidine gluconate, might be beneficial
b. Potential medical complications can usually be identified by obtaining a thorough medical and dental history, by obtaining vital signs, and by appropriate medical consultation.
c. Determine the location of the vascular access arm (hemodialysis) or peritoneal. There are few contraindications to dental treatment in peritoneal dialysis.
d. Avoid using the arm with vascular access for obtaining blood pressure or administering medications.
e. Oral infections should be identified and eliminated using therapy that is as conservative and noninvasive as possible.
f. It is usually recommended that dental treatment be performed the day after hemodialysis to minimize the risk for systemic infection, although some additional bleeding may occur due to presence of residual heparin in the bloodstream.
g. When possible, prescribed medications should be those metabolized in the liver. These include acetaminophen, codeine, and local anesthetics. Drugs metabolized in the kidney will remain in the bloodstream for prolonged periods. Although normally metabolized in the kidney, nonpotassium penicillin is well tolerated and not toxic even if large quantities accumulate in the blood.
h. Following transplantation, it may be necessary to defer definitive dental treatment for 2 months to allow for adequate healing and transplant outcome evaluation. Decisions regarding this should be made in coordination with the patient's physician. Currently, there are no clinical studies that validate the benefit of prophylactic antibiotic coverage in transplant recipients.
i. The complications most likely to be encountered during or following dental treatment are systemic infection, postoperative hemorrhage, or signs of cardiovascular disease or stroke. If systemic infection is suspected, the patient should be referred immediately to his/her treating physician or to a hospital emergency room. Under most circumstances, postoperative hemorrhage relative to dental treatment can be managed using local measures such as primary wound closure, direct pressure, foamed gelatin, synthetic collagen, tranexamic acid or EACA mouth rinses. The patient should not leave the office until clot stability has been established. If local measures fail to control the hemorrhage, referral to a hospital emergency room is indicated.
j. The EMS should be activated if signs or symptoms of a medical emergency such as cardiovascular collapse or stroke become evident.
k. Some evidence indicates that patients with renal disease are less susceptible to dental caries, possibly due to plaque inhibition related to increased levels of salivary urea.
l. The risk for periodontal disease appears to be markedly increased in individuals with severe renal disease or in those receiving hemodialysis. This may be due to increased levels of salivary calculus, patient inattention to dental hygiene procedures, and exaggerated inflammatory response associated with alterations in host defense mechanisms. Secondary hyperparathyroidism may result in accelerated bone loss in the presence of periodontal disease. Conversely, individuals with successful renal transplants may not be more susceptible to periodontal infection than the general population, based on current studies. However, the immunosuppressant drugs used by these patients may mask usual signs of inflammation, and consequently, careful and frequent periodontal evaluation is necessary.

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CLINICAL PROTOCOL 23

Oral Health Care Management for the Pregnant Dental Patient

Pregnancy Synopsis

Significant maternal changes occur during pregnancy. Cardiac output increases 30 to 50%. Cardiac murmurs are common but usually do not require infective endocarditis

prophylaxis. Abdominal contents may press on the diaphragm causing breathing difficulties. Nausea and vomiting/morning sickness occurs in approximately 50 to 90% of all pregnancies. Potential complications may include:

1. **Supine hypotensive syndrome,** which occurs when the gravid uterus partially obstructs the inferior vena cava, decreasing cardiac return to the right side of the heart. This can cause hypotension, syncope, decreased placental blood supply, and diminished oxygen for the fetus. Approximately 10% of females near term show signs of hypotension, light headedness, pallor, and tachycardia when in a supine position.
2. **Gestational diabetes** in approximately 13% of all pregnancies
3. **Hypertension** in approximately 10% of pregnant individuals
4. **Preeclampsia**, a potentially life-threatening condition of unknown etiology, occurs in approximately 5 to 8% of all pregnancies, usually after the 20th week. It features a rapid rise in blood pressure, increased protein in the urine, and edema. Risk factors include preexisting hypertension, diabetes, obesity, and age less than 20 or more than 35. If untreated, it may lead to **eclampsia** with severe convulsive seizures, cerebral hemorrhage, encephalopathy, and other conditions that can result in death of the mother and fetus.
5. **Medication use:** Ideally no drug should be administered during pregnancy, especially in the first trimester. Studies of drug use during pregnancy have resulted in an FDA drug classification system that includes:
   - **A -** remote possibility of fetal harm
   - **B -** No known contraindications but insufficient information to confirm
   - **C -** Animal studies suggest potential harm to the fetus but insufficient human studies have been performed. Use only if potential benefits justify the risk to the fetus
   - **D -** There is positive evidence of human fetal risks.
   - **X -** Drugs are absolutely contraindicated in women who are or who may become pregnant.
6. **Altered oral health**. Pregnant females may experience an increased incidence of gingivitis (pregnancy gingivitis—gingival enlargement), altered subgingival plaque composition, pyogenic granuloma formation, possibly periodontitis, increased tooth mobility, xerostomia or sialorrhea (excessive salivation), dental erosion (due to morning sickness), possibly dental caries (due to neglect in plaque control and nutritional changes), and oral complications associated with pregnancy such as gestational diabetes mellitus or gastroesophageal reflux. Some studies suggest that poor oral health *may* place the patient at increased risk for still birth, premature birth, or low birth weight infants.

Dental Management Principles

1. Preventing treatment problems: A thorough medical and dental history is necessary to fully understand the risks involved in dental care. Information should be obtained regarding pregnancy complications, previous miscarriages, recent episodes of cramping or spotting, and pernicious (severe, excessive) vomiting. It is essential to establish a healthy oral environment early in pregnancy and sustain that throughout. Management of emergent care is essential followed by a preventive program that may include nutritional counseling, rigorous plaque control, frequent dental visits, placement of necessary restorations, and nonsurgical periodontal therapy as often as necessary to maintain periodontal health even in the presence of pathologic pockets. Necessary treatment procedures should be short; minimal amounts of drugs should be administered as necessary to achieve required therapeutic outcomes, and treatment should be performed in a calm, relaxed atmosphere.
2. If dental radiographs are necessary, they should be obtained using the minimal radiation exposure required and after draping the patient in a protective lead apron shield.
3. Antibiotics: Antibiotic prophylaxis is *not* usually required unless the patient presents with medical conditions requiring protective coverage. However, if needed for the well being of the patient, certain antibiotics may be prescribed (category B) although they are capable of passing the placental barrier. These include penicillins, erythromycin (avoid estolate form), cephalosporins, and clindamycin with caution since the drug can be concentrated in fetal bone, spleen, lung, and liver. Antibiotics that are contraindicated include tetracyclines (category D), metronidazole (category C—possibly carcinogenic in animals), clarithromycin (category D), and probably gentamycin and vancomycin (category C).
4. Profound local anesthesia is essential for painful treatment procedures. Local anesthetics will cross the placental barrier and consequently the quantity administered should be the minimal required to achieve profound anesthesia in small areas. Lidocaine, prilocaine, etidocaine, and articaine are in category B and appear to be safe for use. Mepivacinae, bupivacaine, and procaine are in category C and should only be used after physician consult.
5. Supine hypotensive syndrome: In later stages of pregnancy, the position of the pregnant patient becomes critical because of the anatomical changes and pressures on the diaphragm and respiratory system. This should be alleviated by placing the reclining patient on her left side with her right hip elevated 10 to 12 cm using a folded towel, avoiding a completely supine position.
6. Patients who suffer from morning sickness or frequent nausea and vomiting should be advised to rinse their mouths after the event using baking soda and water to neutralize the acidic condition caused by the emesis.
7. Office emergencies: In the event the pregnant patient becomes severely apprehensive, ill, faint, disoriented, or experiences other medical complications, the procedure

should be discontinued, oxygen administered, and the chair properly positioned for management of the immediate problem. The dental staff should be alerted and one should be prepared to activate the EMS if that becomes necessary.

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CLINICAL PROTOCOL 24

Tobacco Cessation

The 5 A's

Ask and document tobacco use for every patient. If the patient continues to use tobacco, discuss any progress toward quitting at the recall appointment.

Advise tobacco users to quit. In a clear, strong, and personalized manner, urge every tobacco user to quit. Advice should be:

- Clear—"I'm sure you know how important it is to quit smoking (or using chewing tobacco)."
- Strong—"As your hygienist, it is my professional obligation to let you to know that quitting tobacco use is the most important thing you can do to protect your oral health, general health, and the health of others in your household. Are you open to talking about your tobacco use?"
- Personalized—Tie tobacco use to current symptoms and health concerns, and/or its social and economic costs, and/or the impact of tobacco use on children and others in the household. "Quitting smoking can improve your oral health (i.e., periodontal disease, implant success, healing, staining, halitosis)."

Assess willingness to make a quit attempt. A nonthreatening way to assess willingness to quit is to use scaling. Ask the patient, "On a scale of 1 to 10, 1 being not at all ready and 10 being ready to quit right now, how would you rate yourself?" If the patient rates himself as a 5, ask, "Why not lower?" This should elicit positive reasons for quitting. The same scale can be used to assess motivation and confidence in quitting. If the tobacco user is willing to make a quit attempt at this time, provide assistance. If the patient clearly states that he or she is unwilling to make a quit attempt at the time, intervention increases future quit attempts. (See "The 5 R's" and Clinical Protocol #27 "Motivational Interviewing for Behavior Change.")

Assist the patient willing to make a quit attempt. Medication can ease the withdrawal symptoms associated with nicotine dependence. All smokers making a quit attempt should be offered medication, except when contraindicated or in specific populations for whom there is insufficient evidence of effectiveness (i.e., pregnant women, smokeless tobacco users, and adolescents). If there are time constraints, provide cessation workbooks, online sites and/or referral to a quitline. The National Quitline number is 1-800-QUIT-NOW If time permits, assist patients in identifying what they have learned from previous quit attempts and what helped, what hurt in previous quit attempts, the challenges they face, and triggers that may prompt tobacco use. Build on past success. Quitting is more difficult when there are other smokers in the household. Patients should encourage housemates to quit with them or to not smoke in their presence. Because alcohol is associated with relapse, the patient should consider limiting/abstaining from alcohol while quitting. Communicate your belief in the patient's ability to successfully quit tobacco use. For patients unwilling to quit at this time, provide interventions designed to increase future quit attempts. (See "5 R's" and Clinical Protocol #27.)

Arrange follow-up. For the patient willing to make a quit attempt, arrange for follow-up contact beginning within the first week after the quit date. If office follow-up is not feasible, recommend counseling in your area, the national quitline network (1-800-QUIT-NOW), local/state/tribal health departments/quitlines and online quit support. For patients who are abstinent, congratulate them on their success. If tobacco use has occurred, review circumstances and elicit recommitment to total abstinence. Consider use of or link to more intensive treatment.

For patients unwilling to make a quit attempt at the time, employ the 5 R's and provide a supportive clinical environment. "I'm available to assist you when you are ready."

Preventing Relapse in Patients Who Have Recently Quit

A former tobacco user should be congratulated on any success and strongly encouraged to remain abstinent. Inquire about specific challenges the patient has encountered and solicit input on how these might be met. If the patient reports prolonged craving or other withdrawal symptoms, consider extending the use of an approved medication or adding/combining medications to reduce withdrawal symptoms.

The 5 R's

Relevance: The dental hygienist should identify and communicate the oral findings related to smoking and encourage the patient to verbalize their most important reasons to consider quitting. This information has the greatest impact if it is relevant to a patient's disease status or risk, family or social situation (e.g., having children in the home), health concerns, age, gender, and other important patient characteristics (e.g., prior quitting experience, personal barriers to cessation).

Risks: The clinician should ask the patient to identify potential negative consequences of tobacco use. The clinician may suggest and highlight those that seem most relevant to the patient. The clinician should emphasize that smoking low-tar/low-nicotine cigarettes or use of other forms of tobacco (e.g., smokeless tobacco, cigars, and pipes) will not eliminate these risks. Examples of acute

risks include shortness of breath, exacerbation of asthma, increased respiratory infections, harm to a developing fetus, impotence, and infertility. Long-term risks include heart attack, stroke, lung and other cancers, chronic bronchitis, emphysema, osteoporosis, long-term disability, and need for extended care.

Environmental risks include increased risk of lung cancer and heart disease in cohabitants, increased risk for low birth weight, sudden infant death syndrome (SIDS), asthma, middle ear disease, and respiratory infections in children in smoking households.

Rewards: The clinician should ask the patient to identify potential benefits of stopping tobacco use. The clinician may suggest and highlight those that seem most relevant to the patient. Examples of rewards are as follows:

- Improved health
- Food will taste better
- Improved sense of smell
- Saving money
- Feeling better about oneself
- Home, car, clothing, and breath will smell better
- Setting a good example for children and decreasing the likelihood that they will smoke
- Having healthier babies and children
- Feeling better physically
- Performing better in physical activities
- Improved appearance, including reduced wrinkling/aging of skin and whiter teeth

Roadblocks: The clinician should ask the patient to identify barriers or impediments to quitting and provide treatment (problem solving, counseling, medication) that could address barriers. Typical barriers might include

- Withdrawal symptoms
- Fear of failure
- Weight gain
- Lack of support
- Depression
- Enjoyment of tobacco
- Being around other tobacco users
- Limited knowledge of effective treatment options

Repetition: The motivational intervention should be repeated every time an unmotivated patient visits the clinic. Tobacco users who have failed in previous quit attempts should be told that most people make repeated quit attempts before they are successful.

Nicotine Dependence

Nicotine satisfies the criteria for drug dependence, which includes compulsive use, psychoactive effects, and drug-reinforced behavior. Additional criteria include stereotypical patterns of use, use despite knowledge of harmful effects, relapse during abstinence, and recurrent cravings. Dependence-producing drugs produce tolerance or the need for the drug in greater quantities to achieve the same effect, physical dependence, which is characterized by unpleasant physiological effects if the drug is unavailable, and a pleasant or euphoric state when the drug is delivered. It is clear from these criteria that tobacco satisfies the criteria for dependence.

Given the implementation of smoke-free workplaces, restaurants, bars, etc., the number of cigarettes per day is not necessarily an accurate measure of the patient's level of nicotine dependence. Using a multifaceted nicotine scaling system can yield more useful results.

The Fagerstrom Test for Nicotine Dependence (FTND) has been widely used to assess the patient's level of nicotine dependence. It was developed to assess only physical dependence. It is particularly useful in patients who have reduced the number of cigarettes per day either by choice or as a response to smoke-free environments.

Fagerstrom Test for Nicotine Dependence

How soon after you wake up in the morning do use tobacco? Score_____

Within 31 to 60 minutes score "1"
Within 6 to 30 minutes score "2"
Within 5 minutes score "3"

Do you find it difficult not to use tobacco where it is forbidden? Score_____

Yes score "1"; no score "0"

What cigarette of the day is the most satisfying? Score_____

First cigarette in the morning score "1"; any other score "0"

How much tobacco do you use per day? Score_____

Cigarettes: Numbers per day _____
10 or less a day score "0"
11- to 20-day (1 pack) score "1"
21 to 30 per day score "2"
31 to greater than 31 score "3"

Do you use tobacco more during the morning than the rest of the day? Score_____

Yes, score "1"; no score "0"

Do you use tobacco when you are sick enough to have to stay in bed? Score_____

Yes, score "1"; no score "0"

Do you inhale/swallow? Score_____

Always score "3"
Often score "2"
Occasionally score "1"
Never score "0"

Total Score _____
A score of 7 or higher indicates high level of nicotine dependence.

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Tobacco Cessation Pharmacotherapy

Medication	Cautions/Warnings	Side Effects	Dosage	Use	Availability
Bupropion SR 150	Not for use if you: Use MAO inhibitor Use bupropion in any other form Have a history of seizures Have a history of eating disorders FDA Boxed Warning: See the FDA Web site for more information	Insomnia Dry mouth	Days 1–3: 150 mg each morning Days 4–end: 150 mg twice daily	Start 1–2 weeks before quit date; use 2–6 months	Prescription only: Generic Zyban Wellbutrin SR
Nicotine Gum (2 or 4 mg)	Caution with dentures Caution with TMJ disorders Do not eat or drink 15 minutes before or during use	Mouth soreness Stomach ache	1 piece every 1–2 hours 6–15 pieces/day If ≤24 cigarettes: 2 mg If ≥25 cigarettes/day: 4 mg	Up to 12 weeks or as needed	OTC only: Generic Nicorette
Nicotine Inhaler	May irritate mouth/throat at first (but improves with use)	Local mouth and throat irritation	6–16 cartridges/day Inhale 80 times/cartridge May save partially used cartridge for next day	Up to 6 months; taper at end	Prescription only: Nicotrol inhaler
Nicotine Lozenge (2 or 4 mg)	Do not eat or drink 15 minutes before or during use One lozenge at a time Limit 20 in 24 hours	Hiccups Cough Heartburn	If smoke ≥30 minutes after waking: 2 mg If smoke ≤30 minutes after waking: 4 mg Weeks 1–6: 1 every 1–2 hours Weeks 7–9: 1 every 2–4 hours Weeks 10–12: 1 every 4–8 hours	3–6 months	OTC only: Generic Commit Mini-Lozenge
Nicotine Nasal Spray	Not for patients with asthma May irritate nose (improves over time) May cause dependence	Nasal irritation	1 “dose” = 1 squirt per nostril 1–2 doses per hour 8–40 doses per day Do NOT inhale	3–6 months; taper at end	Prescription only: Nicotrol NS
Nicotine Patch (7, 14, 21 mg)	Do not use if you have severe eczema or psoriasis	Local skin reaction Insomnia	One patch per day If ≥10 cigarettes/day: 21 mg 4 weeks, 14 mg 2–4 weeks, 7 mg 2–4 weeks	8–12 weeks	OTC or prescription: Generic Nicoderm CQ Nicotrol

(*Continued*)

Tobacco Cessation Pharmacotherapy *(continued)*

Medication	Cautions/Warnings	Side Effects	Dosage	Use	Availability
Varenicline	Use with caution in patients: With significant renal impairment With serious psychiatric illness Undergoing dialysis FDA Boxed Warning: See the FDA Web site for more information	Nausea Insomnia Abnormal, vivid or strange dreams	Days 1–3: 0.5 mg every morning Days 4–7: 0.5 mg twice daily Day 8–end: 1 mg twice daily	Start 1 week before quit date; use 3–6 months	Prescription only: Chantix
Combinations: 1. Patch + bupropion 2. Patch + gum 3. Patch + (lozenge or inhaler)	Only patch + bupropion is currently FDA-approved Follow instructions for individual medications	See individual medications above	See individual medications above	See individual medications above	See above

Based on Clinical Practice Guideline Update: Treating Tobacco Use and Dependence, U.S. Public Health Service, May 2008.

CLINICAL PROTOCOL 25

How to Utilize Nutrition Counseling in Practice

Nutritional counseling is an integral component of the practice of dentistry. The following provides some basic techniques that can be incorporated to enhance the standard of care in the practice of dentistry.

Identifying Patients at Oral Risk Due to Dietary Intake or Habits

1. Assess/collect baseline data
   - Comprehensive medical and dental history
   - Extraoral/intraoral clinical exam
   - Dental charting
   - Periodontal assessment
   - Clinician administered nutrition screening form
2. Obtain useful information from patients
   - Fluoride sources
   - Sensitivity due to heat, cold, or pressure
   - Problems with dry mouth
   - Plaque index score
   - Food allergies, special diet, food dislikes
   - Pertinent medical history
   - Typical daily routine or any factors that impact dietary choices
3. Recognize the conditions that indicate the patient may benefit from dietary counseling
   - Patients who annually exhibit two or more new caries
   - Children with decayed, missing or filled surfaces (DMFS) ≥ than their age in years
   - Patients with increase in dental caries activity
   - Patients with orthodontic appliances
   - Patients undergoing head/neck radiation
   - Patients on prescriptions that cause dry mouth; or children who are chronically ill and on long-term medications
   - Patients who exhibit a deficiency of one or more food groups in a 24-hour dietary recall
   - Patients who habitually eat snacks or are habitual users of sugared mints, gum, or cough drops
   - Patients who consume acidic beverages on a frequent basis
   - Patients with a plaque score greater than or equal to 40%
   - Patients who experience new carious lesions at regular intervals (i.e. every 6 months)
   - Patients with active periodontal disease
   - Patients with exposed root surfaces
   - Patients with salivary dysfunction
   - Partially or completely edentulous patients; patients with ill-fitting partial or full dentures
   - Patients who present with oral or physical signs/symptoms that suggest a nutrient deficiency
   - Presurgical patients (periodontal or oral)
   - Geriatric patients
   - Postmenopausal patients on medications that cause dry mouth
4. Take into consideration patient motivation and knowledge
   - After recognizing the need for counseling, investigate the patient's awareness of the diet/dental relationship.
   - Determine the patient's motivation level to learn and understand more about the connection between their oral health and their dietary intake.
   - Assess where they are on the continuum of change:
     - **Precontemplation:** "I'm not intending to change."
     - **Contemplation:** "I'm intending to change in the next 6 months."
     - **Preparation:** "I am doing the new habit, but not consistently."

- **Action:** "I am doing the new habit regularly, but for less than 6 months."
- **Maintenance:** "I have maintained the new habit for more than 6 months."

- Educate the patient on the oral systemic relationship.
- Educate your patient on how diet can affect oral health.
- Discuss etiology of caries and the impact of dietary factors.
- Discuss how lack of choices from various food groups can decrease nutrient intake and impact immune function and healing properties of the gingival tissue.
- Ask for constant feedback from patients to make sure they are in total understanding of the information you are providing them.
- This should be done prior to eliciting further dietary information from a patient.

5. Use a 24-hour dietary recall
   - When indicated, a 24-hour dietary recall can provide further insight into patient dietary habits for the dental provider.
   - A 24-hour dietary recall lists all food consumed by the patient the previous day.
   - It helps to determine whether a patient would benefit from doing a more intensive food record.
6. Keep a food record
   - A food record is a learning tool used to gather data about a patient's diet. When the data is combined with information about the periodontal health, caries process, and nutrition, the patient gains a better understanding of the diet-dental relationship.
   - Inform patients to write down everything they eat, drink, and chew for a minimum of 3 days. Include two routine days and one nonroutine day such as a weekend day, holiday, or vacation day.
   - Three days is an acceptable time frame if those days are typical days. Seven days can be overwhelming unless the patient is extremely committed.
   - Record HOW the food was prepared (i.e., raw, cooked, candied, creamed, fried, broiled, baked, etc.)
   - Record time of consumption—WHEN it was consumed
   - Record WHERE it was consumed (if outside the home, e.g., fast food restaurant, cafeteria, etc.)
   - Ask patients to be as specific as possible when listing amounts and "extras" added to their food.

Nutrition services provided in the dental practice should focus on educating the patient about the relationship between diet and dental health. Patients who are medically compromised or in need of more in-depth dietary counseling should be referred to a Registered Dietitian.

Dietary information can be evaluated by utilizing interactive tools on the USDA ChooseMyPlate *Web site at http://www.choosemyplate.gov.* The Food Tracker at *http://www.choosemyplate.gov/supertracker* is an excellent resource. The Dietary Guidelines for Americans can provide further guidance. Recommendations can then be made based on the information gathered and analyzed.

Implementing the Dietary Counseling Session

1. Setting should be conducive to exchange of information and learning
2. Teaching aids are recommended to enhance the learning experience. Recommended sources:
   - American Dietetic Association
   - American Cancer Society
   - American Heart Association
   - American Dental Association
   - United States Department of Agriculture (USDA) Nutrient Database
   - Food and Drug Administration (FDA)
   - Dairy Council
   - National Institutes of Health (NIH)-Office of Dietary Supplements
   - Centers for Disease Control and Prevention (CDC)
3. Use proper communication to facilitate learning.
   - Pace the discussion
   - Use open-ended questions
   - Use layman's terms
   - Encourage patient participation. Have them circle foods in red that may put them at risk for caries.
   - Involve patients in decision making
   - Individualize your recommendations. Keep patients' culture, habits, and personal choices in mind regarding dietary intake.
   - Ask for feedback throughout the discussion.
4. Review the reason you initially decided to look further at the patient's diet as it relates to their oral health risk.
5. Discuss your findings with the patient based on your analysis of their dietary intake. Indicate areas where you recommend making changes.
6. Remember to give positive feedback about the patient's diet also. Suggest changes that will benefit oral health.
7. TOGETHER, come up with a plan of action to achieve the desired changes the patient feels are most important.
8. Set goals to help the patient monitor their progress.
   - Be specific
   - Set short-term goals to reach long-term goals
   - Encourage self-monitoring to track progress
9. Provide guidance on a dental healthy diet.
10. End the session
    - Ask if the patient has concerns, expectations, or needs
    - Give feedback from the session
    - Ideally, another appointment should be scheduled to follow up with the patient.
    - If indicated, the patient could be asked to fill out another food record prior to the next appointment
11. Record pertinent diet-dental information in the patient's chart
    - Motivational factors/needs for seeking dietary counseling
    - Dental/Medical history to include fluoride, sealants, diet limitations, plaque index, and caries assessment summary

- Daily routine, significant habits that affect diet-dental health
- Caries risk information discussed
- Results of the form and frequency evaluation
- Results of dietary evaluation using ChooseMyPlate.gov or other nutrition software
- Action plan for caries prevention to include diet modifications
- Dietary plan to enhance immune function in relation to periodontal health

12. Follow up

- Appointment may be short—perhaps in conjunction with another appointment or separate half-hour appointment.
- Concentrate on areas of patient concern
- Time permitting, briefly evaluate second food diary and provide feedback
- Continue interaction and reinforcement at future recall appointments

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CLINICAL PROTOCOL 26

Helping Relationships for Dental Hygienists

As a dental hygienist, you are in the behavior change and lifestyle business.

For patients to be dentally healthy, you need to be a facilitator to help them assume responsibility for their health. If you are tired of badgering, preaching to, and coercing patients to improve their oral hygiene and dental health, don't despair.

There is a better way. Change your relationship with your patients from mundane to exceptional by becoming a helper.

The exceptional hygienist/patient (helper) relationship is one in which there is an attitude of service present in the helper. The person being helped is a collaborator or partner in the relationship. The helper understands her or his primary role is to use her or his technical excellence and the intangible qualities of her or his humanness, caring, compassion, vulnerability, genuineness, wholeness, respect, valuing, and empathy to help the client or patient heal.

This unique relationship is called a helping relationship. At its heart is learning how to become an exceptional active listener.

Carl Rogers' and Arthur Combs' (both PhD psychologists and pioneers in helping relationships) research shows it is the following beliefs of the helper that are most important in a helping relationship:

- they care about the person
- they are person not thing centered
- they are other-centered, not self-centered
- they have a positive view of people
- they are empathic
- they are nonjudgmental
- they are self-confident
- they truly want to help the person
- they are authentic or congruent in their communications

Keeping their research—that it is the person and his or her beliefs and not methods and techniques that are most important—in mind, the following checklist can help you learn to be an exceptional active listener and helper.

- Practice active listening with friends, family, clerks, coworkers—anyone.
- Let go of distractions when listening
- Let go of preconceptions. Remember Henry Tanner DDS's statement: "I know you believe you understand what you think I said, but I am not sure you realize that what you heard is not what I meant."
- Focus on the person you are listening to. Face him or her squarely. Give your total time and attention.
- Maintain good eye contact—but don't stare.
- Maintain a relaxed, open, attending posture, attentive facial expressions, and attentive voice tone.
- Let your feelings show; if you are surprised, show surprise, if you want to smile, smile, if you want to laugh, laugh, if you are sad, be sad, if you are upset, be upset. Let your face respond to the emotions you are feeling.
- Listen more than you talk. Use "I see," "Yes," "Really," "Mm-hmm," and "Anything else?"
- Use door openers: "Tell me more about that", "Help me understand what you mean", "How do you feel about that?", "Do you want to talk about that?"
- Respond nonjudgmentally, using phrases such as: "You feel...", "What I hear you saying is...", "From where you stand...", "It appears to you...", "Let me see if I understand; you mean...".
- Own your own feelings—use "I" messages instead of "you" messages.
- Remember Omer Reed's phrase, "Speak to the obvious, ask a question," and Mary Osborne's, "Stay in the question". Ask questions that will help your patient think about the answer. Stay away from questions that result in a yes or no answer.
- Be selective with your active listening. Like anything else it can be overused. Do not use it when time is short; when the patient wants an answer, facts or information; when you do not feel like listening; when the time and place do not seem right; when the patient seems uncomfortable with how you are active listening.
- Play with active listening, do not make it a chore. If you make mistakes and don't catch the meaning the patient is trying to convey, they will usually tell you, "No, that's not it", or "I mean that... ", or any of a number of responses. Then you get to try again.

Remember to keep on trying. Learning to listen with deep understanding is a developmental process—it does not happen overnight. In almost any new endeavor, you will hit

a wall fairly soon where you feel discouraged. This is just a part of the process of learning. Keep on going and you will get better and better at listening with deep understanding.

All of the above are helpful, but remember Combs' and Rogers' research—it is the person and his or her beliefs that are most important in helping relationships.

If most of these beliefs (Rogers' and Combs' research) are not present, the helper could use all of the tactics, techniques, or methods in the checklist and still miss listening with deep understanding or be a poor helper.

Remember, you will not be this way all of the time with all people. These conditions only apply when you are trying to be effective in helping relationships. Sometimes, you will not be able to do any of these or just some. To do all of them all of the time is beyond human capabilities.

If you have the intent to help and be of service, these values and beliefs will take you a long way in becoming a facilitator/helper to your patients.

By Lynn D Carlisle DDS, the author of In a Spirit of Caring Revisited and editor and publisher of the Web site In a Spirit of Caring. For more information on how to build exceptional doctor-hygienist- patient-client relationships go to www.spiritofcaring.com and/or order the e-book In a Spirit of Caring Revisited by Lynn D Carlisle, DDS from www.amazon.com. Included in these resources are articles by pioneers in preventive dentistry, Carl Rogers and Arthur Combs.

CLINICAL PROTOCOL 27

Motivational Interviewing for Behavior Change

Behavior change is a personal process, and resistance and ambivalence are part of the process. Patients support what they help create and the responsibility for change lies within them. Motivational interviewing (MI) is a patient-centered approach to facilitate positive health behavior change. Originally developed to address addictive behaviors, it has been successfully employed to address a variety of health behaviors including but not limited to: medication compliance, diet compliance, physical activity, and oral hygiene. The practice of MI is a way of "being" with the patient rather than a skill set. The overarching goals of MI are to (1) ask open-ended questions in such a way as to elicit a discussion with the patient about changing behavior in a positive direction; (2) respond to the patient's statements in such a way as to reinforce change and diminish resistance; (3) evoke the patient's thoughts, hopes, and belief in change to help the patient resolve ambivalence and promote behavior change.

Fundamental to the practice of MI are (a) a collaborative equal partnership that honors the patient's expertise and perspectives; (b) discussion with the patient involving his or her own perceptions, goals, and values to enhance intrinsic motivation for change; and (c) affirming the patient's right and belief for self-direction.

The spirit of MI is based on four major principles: (1) express empathy; (2) develop discrepancy; (3) roll with resistance; and (4) support self-efficacy.

1. **Express empathy:** Accept patients as they are. Unqualified acceptance frees the patient to change. Acceptance is not the same as agreement or approval, but a critical point is listening with respect to the patient's answers. Through skillful reflective listening the dental professional may elicit the patient's feelings and views without judgment, criticism, or blaming. Reluctance and uncertainty from the patient is normal and should be expected.

   "I can share information with you but I'm confident that you have most of the answers."

2. **Developing discrepancy:** Motivation for change is enhanced when the patient perceives discrepancies between their current behavior and their hopes for the future. Developing awareness of consequences helps the patient to examine their behavior. A discrepancy between present behavior and important goals motivates change. The *patient* not the dental professional should present the arguments for change.

   "I want to get dentures but I'm afraid."

3. **Rolling with resistance:** Resistance to change is normal and understandable. The dental professional should avoid arguing for change with the patient, it is counterproductive. The clinician should attempt to understand the patient's resistance. If the patient displays resistance in words or body language, the clinician should avoid confrontation and roll or flow with it. An image frequently associated with rolling with resistance is two partners in a dance. New perspectives are invited during the discussion with the patient but not imposed. The patient is a great resource in finding answers and solutions to motivate their own behavior change. Resistance to change is a signal to the dental professional to respond differently to the patient.

   "I don't think I am ready quite yet."

   "OK, Mr. Brown, what do you see as the next step?"

4. **Support self-efficacy:** The patient's own belief in his or her ability to carry out and succeed with a specific change is a key element in motivation to change. The patient, not the dental professional, is responsible for choosing and carrying out the behavior change. The dental professional's own belief in the person's ability to change becomes a self-filling prophecy.

   "Ms. Smith, you must be so proud of the changes you have made."

Five guiding methods that are used throughout MI are (1) ask open-ended questions; (2) affirm feedback; (3) listen reflectively; (4) summarize, and (5) elicit change talk. The first four methods are used in MI to help patients examine their ambivalence and decide on reasons to change. The fifth method blends and guides the use of the other four methods and helps the patient resolve ambivalence.

1. Open-ended questions cannot be answered with brief answers as "yes", "no" or a single word.

   "Tell me about what you ate and drank yesterday."

2. Affirming feedback is a supportive statement that conveys respect and helps to build rapport. The feedback can come in form of a compliment or statement of appreciation about the client's strengths and efforts.

   "Thanks for coming on time today."

   "I appreciate that you want to talk about your struggle with tobacco use."

3. Reflective listening is a response designed to check that the clinician has understood the patient's words and feelings. Reflective listening prevents misunderstandings and lets the patient know that the dental professional is listening and understanding. It also helps the patient internalize what they have said and helps move the interview forward.

   "You feel defeated since you have tried to take care of your teeth but you're overwhelmed by the amount of dental work we've talked about."

4. Summarizing the statements from the discussion with the patient can be used to clarify and reinforce information. Summary statements can be done throughout the conversation with the patient to assure the patient that the dental professional has been listening carefully, to reinforce what has been said, and to prepare the patient to elaborate further.

   "I've enjoyed talking with you today. You're a determined person and you are interested in preventing more cavities. You've come up with some good strategies that will work for you."

5. Change talk is used to create awareness of discrepancy within the patient and helps them resolve ambivalence. The patient visualizes the pros and cons of change through the use of discrepancy. When the patient can develop discrepancy this leads to a decisional balance, which tips the balance and leads to change. The clinician may ask the patient to discuss the pros and cons of their problem behavior to bring forth the arguments for change. When the patient views more pros for change than cons for staying the same, this tips the balance and leads to change. One way to evoke change talk is to ask open- ended questions per the above information. Change talk falls into four categories:

   a. Disadvantages of the status quo

   "**What do you think will happen if you don't change anything?"**

   "I don't want to get more cavities."

   b. Advantages of change

   "What is the advantage of making this change?"

   "I would get fewer cavities."

   c. Optimism about change

   "How confident are you that you can change?"

   "I could probably drink fewer Cokes."

   d. Intention to change

   "So what do you think you intend to do?"

   "I'm going to change when I brush my teeth."

Remember that MI is a process in which the dental professional and the patient share in making behavior change decisions. It is a voyage of discussion, exploration, and negotiation. It is a discussion that involves the complicated opinions, involvement, and equal power of two partners. MI requires the dental professional to be flexible and have the capacity to tolerate uncertainty, the patience to allow silence to generate thoughtfulness, and the ability to refrain from providing solutions or arguments for change.

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CLINICAL PROTOCOL 28

Saliva Testing

Functions of Saliva

Lubrication, eating, chewing, swallowing, talking, protective mechanism, PH maintenance, microbial control, taste mediation, and digestion.

Main Source

Three pairs of major salivary glands: parotid, submandibular, and sublingual.
Other sources: numerous minor salivary glands—all locations except anterior hard palate and gingiva.

Causes of Salivary Gland Hypofunction

Drug side effects; radiotherapy; autoimmune diseases (e.g., Sjögren syndrome) and other systemic conditions (von Bültzingslöwen et al., 2007).

Causes of Salivary Gland Hyperfunction

Drugs; oral conditions; some systemic conditions

Indications for Salivary Flow Test

If the patient complains of any one of the following symptoms:

1. Dry mouth for more than 3 months.

2. Recurrent or persistently swollen salivary glands.
3. Needs liquid to swallow dry foods.

Protocol for Saliva Flow Test

1 empty preweighed 50 mL Falcon tube
1 preweighed Falcon tube with paraffin wax in it.
Stopwatch
1 weighing scale

Method

Unstimulated saliva

- It is best that the test is completed in the morning. The patient must be NPO at least 1.5 hours before the test.
- After seating the patient comfortably in the dental chair he/she should be told to first swallow all the saliva in the mouth.
- The patient should lean the head forward for the test.
- Then for the next 5 minutes, the patient should spit whatever saliva is produced into the preweighed empty Falcon tube. Patient must not talk during this time.
- After 5 minutes, the Falcon tube with saliva collected in it is to be weighed again.
- The weight of the empty Falcon tube before saliva was collected is to be subtracted from the weight after collection of saliva.
- The number is to be multiplied by 3 to get the amount of unstimulated saliva that the patient is able to produce in 15 minutes.
- Normal value: greater than 1.5 mL/15 minutes
- It is generally accepted that when glandular fluid production is decreased by about 50%, a person will have symptoms of dry mouth.

Stimulated saliva

- After the unstimulated saliva test is completed, the patient should again be told to swallow all the saliva in the mouth.
- Then the paraffin wax from the preweighed Falcon tube should be given to the patient to chew on.
- For the next 5 minutes again the patient should be told to spit whatever saliva is produced into the preweighed Falcon tube and keep chewing on the paraffin wax.
- At the end of 5 minutes, the patient is to spit all the saliva as well as the paraffin wax in the Falcon tube.
- The initial weight of the Falcon tube is subtracted from the new weight with saliva.
- The number is to be multiplied by 3 to get the amount of stimulated saliva that the patient is able to produce in 15 minutes.
- Normal value: greater than 10 mL/15 minutes

Measuring saliva using Lashley cup

A Lashley cup is used to measure salivary flow from the parotid gland.

- The inner circular chamber of the Lashley cup is connected to a plastic tube for the collection of parotid saliva.
- The cup is placed over the Stensen duct.
- The outer chamber is connected to a rubber bulb which is squeezed to create negative pressure that maintains the cup in place without movement.
- Saliva coming out of the parotid is collected in a cup.
- Mean unstimulated saliva flow rate from parotid is 0.66 mL/15 mL to 0.94 mL/15 minutes; stimulated flow rate is between 2.44 mL/15 min to 4.36 mL/15 minutes (Elishoov et al., 2005).

Biopsy is considered the gold standard for detecting oral cancer, but recent advances have been made in utilizing saliva as a diagnostic tool that may change this paradigm in the future (Ebbing 2010). Early detection is the key to successful treatment with 5-year survival for oral cancers. In studies completed on patients with oral cancer, elevated levels of certain salivary proteins have been identified (Jokerst, 2009; Hu, 2008). For example, one of the proteins that has been increased in oral cancer is interleukin-8 protein (Tan, 2008). The biggest challenge is to find a test for salivary protein that will be inexpensive and can be used for mass screening (Ebbing, 2010).

Recently an optical salivary sensor has been developed at UCLA by a team of researchers from the engineering and oral biology department with support from NIH. It is programmed to bind to the protein of interest such as interleukin-8. In experiments, it has been found to be 100 times more potent than ELISA. It has successfully detected the IL-8 protein in saliva samples from 20 oral cancer patients (Tan, 2008). Because of the noninvasive advantages of this type of salivary diagnostic test, earlier diagnosis of oral cancers may improve for patients presenting with oral lesions.

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GLOSSARY

Abfraction: Loss of tooth structure caused by biomechanical forces, such as mastication or bruxism.

Ablated (ablation): Removal of a body part or the destruction of its function.

Abrasion: Wearing away of the superficial layers of the mucosal surface by mechanical means.

Abscess: Area of infection comprising dead and dying microbes, white blood cells, and necrotic tissue formed by liquefactive necrosis.

Acantholysis: Rounding and loss of cohesion between epidermal cells or keratinocytes because of loss of intercellular cement substances or faulty formation of desmosomes.

Acanthosis: Thickening of the epithelium.

Acanthosis nigricans: Thickened, hyperpigmented skin occurring on the neck, under the arm, in the groin, and other areas, common in diabetes and some other endocrine disorders.

Acidosis: An acidic pH, under 7.4, in the arterial blood.

Acquired immunity: Immunity that is created in response to specific antigens and not part of the innate immune system.

Acrochordon: Commonly referred to as a skin tag. Skin tags are usually flesh colored, are benign, and pose no risk to the person.

Acromegaly: A disorder caused by oversecretion of growth hormone after puberty characterized by enlargement of the hands, feet, head, and face; organs may enlarge, and metabolic disorders such as diabetes mellitus may occur.

Actinic cheilitis: The term actinic denotes solar involvement, and cheilitis denotes inflammation of the lip. Actinic cheilitis is solar damage, and these tissue changes in the lip region are considered a premalignant condition.

Actinic keratosis: A premalignant condition involving the sun-exposed areas of skin resulting in a "wart-like" lesion forming a hyperkeratotic surface.

Actinomycosis: An infection caused by *Actinomycosis israelii* that produces destructive abscesses that have the characteristic "sulfur granules" in the pus contained in the abscess.

Active immunity: Immunity in which the host is able to produce its own antibodies.

Acute inflammation: Process in which vascular and exudative processes are apparent and the cardinal signs of inflammation are present.

Adenocarcinoma: A tumor arising from glandular epithelium.

Adenomatoid odontogenic tumor (AOT): An encapsulated benign epithelial tumor. Encapsulated in a dense fibrous connective tissue and creates damage by expansion.

Adenohypophysis: Anterior portion of the pituitary gland.

Adhesion: Process in which leukocytes "stick" to the walls of the blood vessels before emigration through the endothelium.

Adjuvant therapy: Additional treatments that increase the effectiveness of the primary therapy or a therapy that is intended to prevent a recurrence of the original disorder.

Advanced glycation end products: Substances produced by adding glucose to proteins, lipids, and other substances in the process of glycosylation.

Agranulocytes: Nongranular leukocytes.

Albers-Schönberg disease (osteopetrosis): A rare bone disease affecting the skeleton and resulting in an absence of bone resorption because of reduced osteoclastic activity.

Allele: Genes that occupy the same locus on paired chromosomes.

Alopecia: Hair loss.

Alternative pathway: Activation of the complement system through immune complexes or bacterial endotoxins.

Alveolar osteitis: Inflammation of the alveolar process after an extraction; "dry socket."

Amalgam tattoo: Amalgam fragments inadvertently incorporated into the oral tissues during restorative or surgical procedures that appear as blue/black focal areas.

Amelanotic melanoma: A light-colored or flesh toned–color melanoma is amelanotic.

Ameloblastoma: The most commonly occurring odontogenic tumor. The tumor is of epithelial odontogenic origin.

Ameloblastic fibroma: A mixed odontogenic tumor composed of neoplastic epithelium and neoplastic myxomatous connective tissue. They are usually associated with third molars.

Anaphylactic reaction: Type I hypersensitivity reaction that is mediated by IgE and may manifest as a severe systemic reaction or a less severe localized reaction.

Anaplasia: Loss of cellular identity and specificity because of structural changes within the cells.

Anemia: A decrease in the number of erythrocytes or in the amount, structure, or function of hemoglobin.

Aneuploid: An abnormal number of one or more chromosomes but not a multiple of a full set or complement of 23 chromosomes.

Aneurysm: A bulging in the wall of an artery caused by a congenital or acquired weakness in the wall.

Aneurysmal bone cyst: A pseudo cyst that, unlike a true cyst, does not have an epithelial-lined lumen.

Angina: Severe, suffocating pain that is normally felt in the chest but may radiate to the left arm, shoulder, and/or jaw and that is associated with cardiac ischemia.

Angioedema: A localized edema involving deeper layers of the skin and subcutaneous tissues that occurs suddenly as an allergic response to foods, medications, or substances found in the environment.

Angiogenesis: Creation of new blood vessels from endothelial cells.

Angular cheilitis: Also known as perlèche.

Angular stomatitis: Also known as angular cheilitis or perlèche.

Ankyloglossia: Condition in which the tongue is bound to the floor of the mouth because of a short lingual frenum attachment close to the tip of the tongue. Mobility of the tongue is decreased or limited.

Ankylosis: The stiffening of a joint as the result of abnormal bone fusion; to become joined or consolidated.

Anodontia: Absence of all teeth.

Anogenital: Relating to the anus and genitals.

Anorexia: Loss of appetite.

Antibody: Immunoglobulin produced by B lymphocytes.

Antifungal: Agent used to destroy or inhibit the growth of fungi.

Antigen: Foreign substance that can provoke an immune response.

Antigen-binding fragment (Fab): Area on the antibody molecule that binds with an antigen.

Antigen-presenting cell: Cell, such as a macrophage, that is able to bring an antigenic substance to a lymphocyte to activate the lymphocyte for that antigen.

Antipruritic: Medications and treatments directed toward controlling skin irritations involving "itching."

Aphthous ulcers: Ulcerations that affect the oral mucosa and are triggered by certain factors such as sunlight, trauma, and stress.

Apoptosis: Normal cellular death to maintain correct numbers, remove old or nonfunctioning cells, or to remove abnormal cells.

Argyria: The bluish-gray color produced by silver salts in the tissues.

Arteritis: Inflammation of one or more arteries.

Ataxia: Jerky, uncoordinated movements.

Atelectasis: Collapsed lung.

Atopic reaction: Type I hypersensitivity reaction associated with symptoms of urticaria, asthma, runny nose and watery, itchy eyes.

Atopic/atopy: Genetically linked hypersensitivity to environmental allergens.

Atrophic: Tissue demonstrating thinning of the epithelium.

Atrophy: An adaptive change that causes an abnormal decrease in the size of a cell.

Atypical: A variation of normal.

Aura: Subjective symptoms that present before an event such as a migraine headache or an epileptic seizure.

Autoimmune disease: Immune system dysfunction in which the immune system produces antibodies against the body's own cells.

Autoimmune thyroiditis (Hashimoto thyroiditis): A group of inflammatory disorders of the thyroid gland that cause destruction of the follicular cells, and therefore, hypothyroidism. Hashimoto thyroiditis is a specific form of autoimmune thyroiditis.

Autoinoculation: Moving an infectious organism from one part of the body to another by physical contact, such as from hands to mouth or eyes.

Autonomic neuropathy: A decrease in the function of the nerves of the autonomic nervous system resulting in less sensitivity and decreased function.

Autosomal: Refers to any of the 22 chromosomes other than the sex chromosomes and any of the genes located on these 22 chromosomes.

Bacteremia: The presence of bacteria in the circulating blood.

Barr body: Chromatin material from the inactivated second X chromosome located near the nuclear membrane of all diploid cells in females.

Basal cell carcinoma: The most common skin cancer. The cancer evolves from the basal cell layer of the epidermis, resulting in invading nests and strands of neoplastic basal cells.

Basal keratinocytes: Basal keratinocytes are epithelial cells that produce keratin. In pigmented lesions, the melanocyte transfers melanin to the keratinocytes.

Basal metabolic rate (BMR): The amount of energy required to maintain the body in a resting state.

Basophil: A granular leukocyte with an irregular shaped, two-lobed nucleus.

Behçet syndrome: Affects multiple organs including the heart, central nervous system, the eyes, and gastrointestinal site. Aphthous ulcers are common with the syndrome.

Benign: A mild condition or illness or a neoplasm that grows locally and does not metastasize.

Benign nevus: A nonmalignant overgrowth of melanocytes occurring at birth or later in life.

Bilirubin: Yellow substance produced when red blood cells are destroyed either during normal cellular replacement or during pathologic destruction.

Biological therapy: A type of treatment used to stimulate or restore the ability of the immune system to fight cancer, infections, or other diseases.

Biomarker: Substance/s found within the body that can be associated with the presence of a malignancy.

Biopsy: A procedure that includes the microscopic study of tissues removed from a suspicious area to determine a definitive diagnosis.

Blastic cells: Immature cells.

Blue nevus: The second most commonly found type of nevus found intraorally. The deep blue color is characteristic, and some have been reported to transform to malignant lesions.

Bohn nodules (gingival cyst of the newborn, dental lamina cysts of the newborn): Tiny nodules along the junction of the hard and soft palate and along dental ridges that are derived from epithelial remnants.

Bone marrow suppression: Inhibition of the production of all solid blood components including white and red blood cells and platelets.

Bossing: A rounded elevation or protuberance.

Botryoid odontogenic cyst: A variant of the periodontal lateral cyst that is seen as a multilocular, grape-like cluster of cysts with the exact characteristics of the periodontal lateral cyst.

Bradykinesia: Slowed or overall decrease in spontaneous movement.

Bradykinin: Powerful chemical mediator that causes vasodilation and increased vascular permeability and stimulates pain receptors.

Bulla/bullae (plural): A blister-like lesion that measures greater than 0.5 cm in diameter.

Café-au-lait macule: Light to dark coffee-colored area of hyperpigmented skin that is distinguished from the surrounding tissues by color alone. The café-au-lait macule is characteristically seen in neurofibromatosis and in some forms of fibrous dysplasia, among other disorders.

Calcifying epithelial odontogenic tumor (CEOT): An epithelial odontogenic tumor also known as the Pindborg tumor.

Calcifying odontogenic cyst (Gorlin cyst): Cyst containing "ghost cells" or keratinocytes without nuclei. Calcifications may be seen within the lesion.

Callus: Overproduction of keratin within the skin as a result of friction.

Cancer grading: System of determining the potential aggressiveness of a malignant tumor by classifying its cells as to their degree of anaplasia and the number of mitotic figures seen in a given sample.

Candidosis/candidiasis: Terms are used interchangeably and given to a disease involving an infection with *Candida* and especially *Candida albicans*. The disease usually occurs in someone who is in a debilitated state.

Carcinogenesis: The process of cancer development.

Carcinogenic agent: Substance that can initiate the development of cancer.

Carcinoma in situ: Epithelial cancer that has not broken through the basement membrane.

Carcinoma: Malignant growth of the tissues derived from the ectoderm.

Cardinal signs of inflammation: Signs that present during acute inflammation: redness, heat, swelling, pain, and loss of function.

Carditis: Inflammation or infection of the heart.

Carrier: Refers to an individual who is heterozygous for a recessive genetic trait or disorder.

Cascade: A series of events in which the product of the first event activates the second event and so on.

Caseous necrosis: A term denoting a necrotic tissue resembling cheese made of a mixture of protein and fat. Caseous granulomas are typically found in tuberculosis.

CD4 count: A measure of the number of helper T cells per cubic millimeter of blood, used to analyze the prognosis of patients infected with HIV.

Cell-mediated reaction: Type IV hypersensitivity reaction that is mediated by the cells of the immune system, not antibodies.

Cellulitis: Inflammation of connective tissue.

Cementoblastoma (true cementoma): A true neoplasm of cementoblasts. The lesions may produce pain, and the tooth remains vital. The cementoblastoma is attached to the tooth root and appears radiographically as an opaque calcified mass.

Cementoosseous dysplasia: A term for three types of lesions: periapical cementoosseous dysplasia, focal cementoosseous dysplasia, and florid cementoosseous dysplasia.

Cementoossifying fibroma: A benign neoplasm composed of cementum-like calcifications and bony components.

Central giant cell granuloma: A reactive or reparative lesion to trauma or local factors. Focal aggregates of small multinucleated giant cells are characteristic.

Centromere: The area that joins two chromatids to form a chromosome and forms the arms of that chromosome.

Cementoma: An older term for periapical cementoosseous dysplasia.

Chancre: In primary syphilis, an ulceration that develops at the site where the spirochete *Treponema pallidum* entered the host approximately 3 to 4 weeks after contact.

Cheilitis: Inflammation of the lips or of a lip, with redness and the production of fissures radiating from the angles of the mouth.

Chemical mediator: Chemicals produced by cells or microorganisms that activate, enhance, or terminate a physiologic action.

Chemocaries: Caries occurring as a result of xerostomia associated with chemotherapeutic agents used in cancer therapy.

Chemokine: Chemical mediator.

Chemotaxis: Movement of cells in response to chemical substances.

Chemotherapy: Method of treating neoplastic disease with chemicals or drugs.

Chondroma: A benign cartilaginous tumor of unknown cause. It is of concern when distinguishing this lesion from the chondrosarcoma because it has some similar characteristics clinically and histologically.

Chondrosarcoma: A malignant tumor of the cartilage.

Choristoma: A well-formed growth of tissue in an area where that tissue is not normally found.

Chromatid: Each one of the two strands of genetic material joined by the centromere during prophase.

Chromatin: The genetic material basic to all life comprising deoxyribonucleic acid or DNA.

Chromosome: Structure that carries the genetic material through all cellular reproductive phases. Numbers of chromosomes are highly specific for each species; humans have 46 or 23 pairs of chromosomes.

Chronic myelogenous leukemia: Form of leukemia in which there is an overproduction of granulocytic forms of white blood cells.

Chronic osteomyelitis with proliferative periostitis: Reactive proliferation of periosteum with inflammation of the bone producing scar tissue.

Cicatrix: Scar.

Circumscribed: Confined within a sharp boundary.

Civatte bodies: Eosinophilic ovoid bodies that are apoptotic (dying cells) or necrotic keratinocytes (epithelial cells that ultimately keratinize) at the basement membrane (observed microscopically).

Classic pathway: Activation of the complement system by means of an antigen/antibody complex.

Clotting system: Cascade that results in the production of a blood clot to stop blood flow.

Coagulation necrosis: Cell death associated with ischemia in which cellular outlines are maintained.

Coalescing/coalesce: The growing together of once separate lesions.

Codominance: Refers to a situation in which traits contained on heterozygous alleles are equally expressed in the individual's phenotype.

Coloboma: An absence or defect of some portion of the tissues of the eye.

Colonoscopy: Medical test to visually screen for cancer and other abnormalities of the colon.

Colostomy: Creating an opening from the skin into the colon through which solid wastes will empty into a bag.

Comedones: Inflamed, dilated hair follicles filled with keratin, bacteria, and sebum. Comedones may be open to the outer skin surface or they may be closed. Common names for them are whiteheads or blackheads.

Complement system: Cascade that results in the formation of chemical mediators or the membrane attack complex.

Complete penetrance: Refers to a genotype that is always portrayed in the phenotype of those with that genotype.

Complication: A disease process or condition occurring during the course of an unrelated disease or condition that may or may not be a result of the conditions caused by the original disease.

Compound nevus: Cells found in both the basement membrane and the connective tissue.

Condylomata lata: Papillary lesions involved in the secondary stage of syphilis.

Congenital: Diseases, conditions, or abnormalities that are present at birth but are not necessarily hereditary.

Contact dermatitis: A type IV cell-mediated hypersensitivity reaction in which skin contact with an antigen produces a localized inflammatory response in the form of a pruritic, vesicular rash (allergic contact dermatitis).

Convergent: Roots of adjacent teeth move or are pushed toward each other.

Coronal: Pertaining to the crown portion of a tooth.

Corrugated: Ridged or washboard-like.

Corticosteroids: Medications that have multiple actions including anti-inflammatory and immunosuppressant effects.

Crepitus: Crackling noises or vibrations felt when palpating an area or lesion.

CREST syndrome: Systemic sclerotic disease that not only exhibits telangiectasias but also Raynaud phenomenon, esophageal dysfunction, sclerodactyly (the skin becomes stiff and smooth), and the formation of cutaneous nodules.

Crusted: Covered by a scab.

Cyst: A fluid-filled cavity lined by epithelium and surrounded by an epithelial-lined cyst wall.

Cystic hygroma: A developmental malformation of lymph vessels located in the submandibular and neck region that can become large enough to cause respiratory distress.

Cytokines: Chemical mediators.

Cytotoxic reaction: Type II hypersensitivity reaction in which tissue cells become antigens and the immune system attacks them.

Cytotoxic virus: A virus that is detrimental or destructive to cells.

Deep fungal infections: Infections that arise from soil, bird and bat droppings, or decaying vegetation. Some organisms reside as normal inhabitants in the body, but may cause problems when they are able to enter the body through tears or cuts in the skin.

Definitive diagnosis: The final determination of the actual cause of a condition.

Deletion: Refers to the loss of a portion of a chromosome.

Demyelination: Loss of the myelin sheath from neurons.

Dental erosion: Loss of tooth structure caused by the action of acidic substances other than products of acidogenic bacteria.

Dentigerous cyst: An odontogenic cyst that arises from a cystic change in the dental follicle following crown formation.

Deoxyribonucleic acid (DNA): Genetic material found in chromosomes.

Depapillated: Atrophy with loss of filiform papillae of the dorsal tongue.

Desquamative gingivitis: The term is used to describe the red, shiny, erythematous gingiva that is often characteristic of certain mucosal disease states. The term is a very general term without a diagnostic value.

Developmental disorder: Usually caused by errors in morphogenesis during conception and fetal growth.

Diabetes mellitus: A metabolic disorder related to either an absence of insulin, or decreased production of insulin, or increased cellular resistance to insulin.

Diabetic dermopathy: A condition that manifests as red, hyperpigmented, papular, well-circumscribed, oval-shaped chronic lesions. These are usually found on the shins but may be found on the thighs and forearms.

Diabetic ketoacidosis: A drop in the pH of the blood caused by a buildup of ketone bodies resulting from the breakdown of stored fats.

Diascopy: Diagnostic tool used to evaluate a suspected vascular lesion.

Differential diagnosis: A list of probable or most likely causes of a particular abnormality.

Differentiation: The degree of specialization seen in the microscopic evaluation of cancer cells.

Diploid: Refers to a cell that contains a full complement of 46 chromosomes or two sets of 23 chromosomes, in the case of the human species, one from each paternal and maternal contributor.

Distal: An area or part located away from the center of the body or origin of a structure.

Divergent: Roots of adjacent teeth move or are pushed away from each other.

Diverticulum/diverticula (plural): A pouch or pocket extending out from a tubular structure like the esophagus or intestine.

Dominant: The one allele in a heterozygous set that is expressed exclusively over the other or recessive allele.

DNA repair genes: Genes that are responsible for making sure the DNA strand within the cell is intact.

Droplet nuclei: Aerosolized moisture containing tuberculosis organisms.

Dysesthesia: A disagreeable sensation produced by ordinary stimuli.

Dyskinesia: Abnormal movements.

Dysphagia: Difficulty in swallowing.

Dysphonia: A change in voice quality or the ability to create sounds.

Dysplasia: Growth of abnormal cells in an abnormal arrangement within the tissue.

Dysrhythmia: Abnormal rhythm.

Ecchymosis: A hemorrhagic spot in the skin or mucous membrane caused by the extravasation of blood into the subcutaneous tissues.

Echocardiogram: The report that results from an ultrasound examination done to diagnose abnormal structure and function in the heart.

Ectoderm: The outermost of the three germ layers present in the developing embryo from which the skin, nails, hair, glands, nervous system, and teeth, among other structures, are developed.

Eczema: Generic term denoting inflammatory conditions of the skin.

Edema: Fluid in tissues from exudation.

Elastosis: The degeneration of collagen fibers, making tissues more expansive.

Electrodesiccation: A high-frequency electrocurrent used to seal off blood vessel supply to the skin.

Embolus/emboli (plural): A blockage that consists of a substance such as a thrombus, clump of bacteria, or other foreign matter that has traveled through the circulatory system to lodge in a vessel.

Embryo: Refers to the early stage of development of an organism, up to the end of the eighth week of gestation in humans.

Emigration: Movement of white blood cells between the endothelial cells in vessel walls out into the surrounding tissues.

Emulsifier: Substance that mixes with fats to allow for their absorption into the body.

Encapsulated: Surrounded by a fibrous capsule.

Endocardium: Endothelial and subendothelial connective tissues in the heart.

Endogenous: Originating from within the body.

Endophytic: Indicates the direction of growth going into the tissues.

Endosteal: A term used to denote the layer of endosteum lining the inner surface of the bone.

Endothelium: A layer of flat cells lining the blood and lymph vessels and the heart.

Eosinophil: Granular leukocyte that contains a nucleus that has two lobes connected by a thread of chromatin.

Ephelides: Ephelides are most commonly known as freckles.

Epicanthal fold: A fold of skin that overlaps the area of the inner canthus of the eye.

Epidermis: The outer layer of the skin.

Epidermolysis acquisita: An acquired form of epidermolysis bullosa. Oral blistering and stripping of the epithelium occurs.

Epidermolysis bullosa: A diverse group of inherited and acquired diseases characterized by fragility of the skin and mucosa.

Epistaxis: Nosebleed.

Epithelial rests: The remains of the epithelial root sheath that cover the roots during root development.

Epithelization: Formation of epithelium over an injured surface.

Erosion: Pathologic thinning or removal of the surface layers of epithelium resulting in a depressed lesion that does not extend into the dermis.

Erosive lesions: Denuded areas that occur above the basal layer of epithelium.

Eruption cyst: A variant of the dentigerous cyst caused by the accumulation of fluid or blood between the crown of an erupting tooth and the reduced enamel organ usually due to trauma.

Erythema/erythematic: An abnormal redness of the gingiva, oral tissue, or skin.

Erythema multiforme: A hypersensitivity reaction characterized by target or "iris" lesions.

Erythrocytes: Red blood cells.

Erythroleukoplakia: Premalignant or malignant lesion consisting of a mixture of both red and white color within the tissue.

Erythroplakia or erythroplasia: A clinical description of a persistent red patch that cannot be characterized clinically as any other condition and is usually in various stages of premalignancy or malignancy.

Erythropoiesis: The process of producing erythrocytes in the bone marrow.

Estimated average glucose (eAG): Expression of the A1C percentage in a more easily understood format (milligrams per deciliter) used on a daily basis by those with diabetes to manage their disease.

Etiology: Cause of a disease or condition.

Euploid: Cells containing the correct number of chromosomes for that organism.

Ewing sarcoma: A malignant bone tumor of unknown origin.

Exacerbate: To make a condition worse.

Excisional biopsy: The complete removal of a tumor or other abnormal area to examine the cellular components to determine whether they are benign or malignant.

Exocrine system: Comprised of glands that secrete through a duct onto the surface of a tissue.

Exogenous: Originating from outside of the body.

Exophthalmos: Bulging of the eye that can be caused by pathology or other condition.

Exophytic: Indicates growth is directed toward the external surface or away from the affected tissue.

Exostosis: Excessive production of bone on the facial surfaces of the maxilla and mandible usually caused by occlusal forces.

Expressivity: Variation in how a particular phenotype is exhibited or manifested.

Exsanguination: Bleeding out.

Exudate: Any fluid that has flowed out of a tissue or its capillaries because of injury or inflammation.

Factitial injury: An injury to the tissue that is self-induced and produced by trauma.

Fasting plasma glucose test: Blood test that measures the blood glucose level first thing in the morning after an overnight fast and before eating.

Febrile: Pertaining to fever.

Fetus: Refers to that stage in the development of an organism after it has attained a recognizable form, in humans from the beginning of the ninth week of gestation until the time of delivery.

Fibrinous exudate: The protein that forms a clot in the process of blood coagulation.

Fibrinous: Tissue that is primarily fibrinous connective tissue.

Fibroblast: Immature fiber-producing cell of the connective tissue that can differentiate into a chondroblast, osteoblast, or collagenoblast.

Fibrous repair: Healing by means of the formation of scar tissue.

Field carcinogenesis: A theory that suggests certain cancers develop within a contiguous field of preneoplastic cells. Cells of a field show genetic alterations associated with the process of carcinogenesis even though the tissues appear clinically normal.

Fine needle aspiration: Method of biopsy using a fine needle to draw cells out of a tumor for microscopic study to determine whether they are benign or malignant.

Fissured/fissure: Deep crevice or crevices.

Fistula: An abnormal passage from one epithelial surface to another.

Fluctuant: Manifesting a wave-like feeling upon palpation.

Focal argyrosis: An older name sometimes used to describe an amalgam tattoo, but because amalgam is not pure silver, it is a somewhat inaccurate term.

Focal melanosis: A pigmented macule that occurs on the oral tissues.

Focal sclerosing osteomyelitis (condensing osteitis): An inflammatory reaction that is usually associated with pulpal inflammation or necrosis.

Foliate papilla: Folds of tissue containing taste buds found along the posterior lateral border of the tongue.

Follicles: Cells of the thyroid that produce the thyroid hormones.

Follicular: Pertaining to the tissues surrounding the developing tooth bud.

Forchheimer sign: Oral lesions evident in early rubella.

Free radical: An atom carrying an unpaired electron.

Gamete: Sex cell (sperm and ovum).

Gardner syndrome: An autosomal dominant disease characterized by gastrointestinal polyps that develop in the colon, stomach, and upper intestine. The syndrome includes the osteoma and sometimes odontomas, epidermoid cysts, supernumerary teeth, other benign tumors of the skin and soft tissues, and multiple polyps.

Gastroesophageal reflux: Backward flow of the acidic contents of the stomach through the muscle sphincter into the esophagus. If severe, stomach contents may regurgitate into the oral cavity.

Gene: The basic unit of inheritance that is found at a specific locus on a chromosome and has a specific function related to the formation of an enzyme or protein essential for development and life.

Generalized: Found in a majority of areas or covering one specific area.

Genokeratosis: Inherited disorders of the skin and oral mucosa.

Genome: All of the genes in a complete set of chromosomes for a specific species, such as the human genome.

Genotype: The actual genetic makeup of an individual consisting of all possible alleles not just those that are clinically observed.

Gestational diabetes mellitus: Diabetes that is first noticed during pregnancy.

Giant cell: Large cell formed by the joining of several macrophages.

Giant cell epulis: Term that is often used interchangeably for a peripheral giant cell granuloma.

Gigantism (giantism): A disorder caused by hypersecretion of growth hormone before puberty that causes overgrowth of the long bones and results in excessive growth of the entire body.

Gingivectomy: Surgical removal of gingival tissue not supported by bone.

Glands of Blandin-Nuhn: One of three primary salivary glands of the tongue. These glands of Blandin-Nuhn are embedded in the musculature of the anterior ventral tongue.

Glandular odontogenic cyst: Derived from odontogenic origins, this cyst is locally aggressive, produces swelling and expansion, and may have histological features similar to those of mucoepidermoid carcinoma.

Glossitis: Inflammation of the tongue.

Glycosylation: The formation of chemical linkages between glucose and other molecules such as hemoglobin.

Goiter: Enlarged thyroid gland caused by hypertrophy or hyperplasia (other than neoplastic growth).

Gonorrhea: A venereal disease caused by the bacterium *Neisseria gonorrhea* gonococcus.

Gorlin sign: The ability to touch the tip of the nose with one's tongue.

Graft versus host disease: Disease that may occur after the initial organ or tissue has been transplanted into the host and may manifest as various types of cutaneous or mucosal lesions including ulcers and erosions involving a specific area or multiple sites.

Granulation tissue: The formation of minute, rounded, fleshy connective tissue projections on the surface of a wound, ulcer, or inflamed tissue undergoing the process of healing.

Granulocyte: A mature granular leukocyte.

Granuloma: A persistent area of inflammation in which the offending agent cannot be removed.

Granulomatous inflammation: A subset of chronic inflammation in which macrophages lose their phagocytic abilities and become similar to epithelial cells.

Graves disease: Autoimmune hyperstimulation of the thyroid follicles resulting in an excessive amount of thyroid hormones.

Gumma: A lesion found in the tertiary stage of syphilis.

Hamartoma: A focal malformation consisting of an abnormal mixture of tissue elements or an abnormal amount or proportion of a single element normally present within a specific site.

Haploid: Refers to cells or gametes containing a single set of 23 chromosomes.

Hapten: Small molecule that must combine with a larger protein molecule in order for the immune system to initiate the production of antibodies against it.

Heart murmur: Abnormal heart sound.

Hemangioma: A congenital anomaly involving the blood vessels, which proliferate and resemble a neoplasm.

Hemarthrosis: Joint pain and deformity caused by bleeding into the joint space usually seen in severe bleeding disorders.

Hematocrit: Measurement of the packed red cell volume as a percentage of whole blood.

Hematoma: A localized mass of extravasated blood that is collected or pooled within an organ or tissue.

Hematopoiesis: The process of producing all blood cells and platelets in the bone marrow.

Hematopoietic system: Blood forming system.

Hematuria: The presence of blood in the urine.

Hemoglobin A1C: The most common form of adult hemoglobin found in red blood cells.

Hemolysis/hemolytic: The breakdown or destruction of red blood cells releasing hemoglobin, or a condition that causes such a breakdown.

Hemoptysis: Coughing up blood in the sputum.

Hemostasis: The cessation of bleeding by the coagulation cascade or by extrinsic mechanical or chemical means.

Heterozygous: Having different allelic genes at one locus or (by extension) many loci; heterotic.

Hepatocellular carcinoma: Liver cancer.

Hereditary hemorrhagic telangiectasia: Autosomal-dominant condition featuring abnormal vascular dilations.

Hereditary (inherited): A trait or characteristic that is passed from generation to generation through genetic material.

Herpes simplex virus (HSV): A member of the human herpes virus (HHV) family known as *Herpetoviridae*.

Herpetic whitlow: A term given to a finger that becomes infected with the herpes simplex virus from a primary or recurrent lesion, thereby producing a vesicle-like infection on the finger.

Herpetoviridae: A family of morphologically similar viruses that is divided into three subfamilies, one of which includes herpes simplex virus, varicella-zoster virus, cytomegalovirus, and the Epstein-Barr virus.

Heterozygous: Condition that occurs when the maternal and paternal genetic alleles, located at a specific locus on the chromosomes, are different.

Hiatal hernia: Protrusion of a portion of the stomach through the hole in the diaphragm through which the esophagus normally passes. This condition predisposes an individual to gastroesophageal reflux.

Histamine: Chemical mediator.

Homeostasis: A normal balance of body systems and functions.

Homologous: Refers to chromosomes that have the identical types of genes contained within them.

Homozygous: Condition that occurs when the maternal and paternal genetic alleles, located at a specific locus on the chromosomes, are the same.

Hormone: Chemical substances secreted by the glands of the endocrine system.

Hormone/antihormone therapy: A form of therapy using hormones to inhibit the growth of tumors by either increasing the amount of hormone present or by blocking the existing hormones.

Human papillomaviruses (HPV), high-risk: High-risk human papillomaviruses are associated with an increased risk of primary malignancy or of malignant transformation of a benign lesion.

Human papillomaviruses (HPV), low-risk: Low-risk human papillomaviruses are associated with benign lesions and are not likely to cause the infected cells to undergo a malignant transformation.

Hutchinson triad: The term used in relation to congenital syphilis resulting in a triad of eye inflammation, deafness, and dental abnormalities.

Hyperacusis: Hypersensitive hearing.

Hyperadrenalism: Excessive production of adrenalin.

Hypercalcemia: Excessive levels of calcium in the blood.

Hypercementosis: Overgrowth of cementum.

Hypercholesterolemia: Abnormally high level of cholesterol in the blood.

Hypercoagulation: Abnormal increased tendency to form blood clots that occlude vessels and cause tissue damage.

Hyperemia: The presence of an increased amount of blood in a body part or organ.

Hyperglycemia: Excessive levels of glucose in the blood.

Hyperosmolar hyperglycemic state: Excessive amount of glucose that causes osmotic changes in the tissues, such as in brain cells causing coma and in kidney cells causing massive loss of water through the urine.

Hyperhidrosis: Excessive sweating.

Hyperinsulinism: Abnormally high level of insulin that is usually associated with hypoglycemia.

Hyperkeratosis: Overproduction of keratin.

Hyperplasia: An adaptive change that causes an increase in the number of cells within a tissue.

Hyperplastic: An abnormal increase in the number of cells in an organ or a tissue with consequent enlargement.

Hyperreflexia: Exaggerated deep tendon reflexes.

Hypersensitivity: An abnormal sensitivity to an agent or a foreign substance.

Hypersensitivity reactions: A condition in which there is an exaggerated response by the body to the stimulus of a foreign agent.

Hypertelorism: Eyes that are spaced abnormally far apart.

Hyperthyroidism: Excessive production of thyroid hormone.

Hypertrophy: An adaptive change that causes an increase in the size of cells within a tissue.

Hyphae: Elongated form of *Candida albicans*.

Hypochromatic nuclei: Nuclear material that is darker or more pigmented than normal.

Hypodontia: Partial absence of teeth.

Hypoglycemia: Inadequate levels of glucose in the blood.

Hypoglycemic unawareness: Condition in which the individual who has diabetes is not aware of the warning signs of hypoglycemia either because they do not feel the symptoms or they are not able to respond to them because of age or mental disability.

Hypoinsulinism: Inadequate amount of insulin in the blood causing hyperglycemia.

Hypophysis: Pituitary gland.

Hypotelorism: Eyes that are spaced abnormally close together.

Hypoxia: Decrease in the amount of nutrients, especially oxygen, available to the cell.

Iatrogenic injury: An injury caused by medical personnel during diagnostic or treatment procedures or because of exposure to a hospital or other healthcare environment.

Idiopathic: Of unknown cause.

Immune complex–mediated reaction: Type III hypersensitivity reaction in which antigen-antibody complexes circulate in the blood and are deposited in tissues where they initiate an inflammatory response.

Immunofluorescence diagnostic test: An immunohistochemical technique using labeling of antibodies by a fluorescent dye to identify antigenic material specific for the labeled antibody. The fibrinogen is accentuated and presents with a particular pattern for a specific disease.

Immunoglobulins: Natural antibodies produced by plasma cells.

Immunosuppression: The depression of the immune response.

Immunotherapy: A form of therapy that uses our own immune systems to combat disease, by initiating a reaction, augmenting a reaction, or by changing our immune reactions.

Impetigo: A highly contagious infection caused by the bacterial organism *Streptococci* or by *Staphylococcus aureus*.

Incisional biopsy: Method of obtaining cells for microscopic examination that removes a piece of the abnormal area or tumor and some normal surrounding tissue.

Incomplete penetrance: Expressed as a percentage of those who possess a particular genotype but do not express the characteristics of that genotype in their phenotype.

Incubation period: Period after exposure to a pathogen and before the manifestation of signs and/or symptoms.

Induration: Hardening of an area of tissue.

Infarction: Area of necrosis caused by a sudden deficiency of blood supply to that area.

Integumentary system: System comprising the skin, mucous membranes, the glands that open onto them, hair, and nails.

Interleukin-1: A cytokine.

Intermediate expression: Occurs when an individual that is heterozygous for a particular trait does not fully express either one of the possible phenotypes but expresses a phenotype that represents a blending or mid range of the two.

Intradermal nevus: A later stage nevus in which the nests of nevus cells are found only within the underlying connective tissue.

Intralesional: Introduced into or performed within a lesion.

Intramucosal nevus: The oral counterpart to the intradermal nevus. The nests of nevus cells are found in the connective tissue.

Inversion: A structural abnormality that occurs when a chromosome breaks at two places and the broken piece is turned around and reinserted at the same location.

Involution: The return of an enlarged organ to normal size.

Ionizing radiation: Radiation sufficiently strong to split molecules into ions causing a high degree of biological damage.

Irritant contact dermatitis: Skin irritation (nonallergic) due to contact with substances or chemicals.

Ischemia: Loss of nutrients, usually oxygen, caused by an obstruction in the flow of blood.

Jaundice: Yellowing of the skin and mucous membranes caused by a buildup of bilirubin in the tissues.

Junctional nevus: A collection of nevus cells (thèques) along the basal cell layer of the epithelium.

Kaposi sarcoma: A malignant neoplasm occurring in the skin, oral tissues, and lymph nodes. The neoplasm is more common in patients who are in debilitated states such as those with AIDS and the elderly.

Karyotype: A photomicrograph of an array of metaphase chromosomes arranged in order of descending size and the position of the centromeres.

Keloid: Excessive scar formation.

Keratin pearls: Spheroidal masses or nests of keratin deep within the epithelium usually associated with malignancy.

Keratinization: Keratin formation of a horny layer; the process whereby epithelial cells lose water and become hard.

Keratinocyte: An epithelial cell that produces keratin, other proteins, and sterols. It is formed at the basal layer from undifferentiated cells and then undergoes progressive changes as it moves toward the surface layer of the skin where it eventually exfoliates.

Keratoconjunctivitis sicca: Chronic severe dry eyes, also called xerophthalmia.

Keratolytic: Relating to or causing keratolysis (breakdown of keratin).

Kindred: A group of related persons; a family. In genetics, multiple generations of a family unit carrying a genetically transmitted characteristic that is used for study of the abnormality.

Kinin system: Cascade that produces chemical mediators such as bradykinin.

Koebner phenomenon: Ability of a disease to affect chronically irritated tissue.

Koilocyte: A vacuolated pyknotic epithelial cell that has either a clear cytoplasm or a perinuclear halo and that tends to be associated with certain human papillomavirus infections.

Koplik spots: Small macules with white necrotic centers appearing on the buccal mucosa of individuals with measles.

Labial melanotic macule: A pigmented macule occurring on the lip.

Labile cells: Cells that undergo replication at a high rate to replace worn out or injured cells of the same type.

Laminar: Arranged in layers as in normal blood flow.

Latent period: Period of time during which no signs or symptoms are observable but the condition may be found by other means.

Langerhans cell disease: Formally called histiocytosis X, involves proliferation of Langerhans cells that normally reside in the epidermis and mucosa. The cause is unknown.

Laugier-Hunziker phenomenon: An acquired, benign macular hyperpigmentation of the lips and oral mucosa often associated with pigmentation of the nails. The disorder may have similar appearances to more serious diseases such as Addison and Peutz-Jeghers.

Leishmaniasis: A cutaneous lesion caused by a protozoan belonging to the genus Leishmania. It is transmitted by the bit of a female phlebotomine sand fly.

Lentigo: A benign freckle-like lesion that results from chronic ultraviolet damage to the skin; also called age spots and lentigo solaris.

Lesion: A wound or a distinct area in which a pathologic change has taken place.

Leukocyte: White blood cell.

Leukocytosis: An abnormal increase in the number of leukocytes over 10,000 mm^3.

Leukopenia: Lower than normal levels of white blood cells.

Leukoplakia: Premalignant lesion presenting as a white plaque without distinguishing clinical features.

Leukotrienes: Chemical mediators.

Libman-Sacks endocarditis: Small nonbacterial vegetations that may form on the valves of the heart and is a medical consideration for patients who have lupus.

Lichen planus: A chronic, unpredictable inflammatory keratotic disease that is a cell-mediated immune response producing tissue lesions. The lesions may be categorized into six different types.

Lichenoid reaction: The reaction caused by sensitivity to a substance such as amalgam, gold, or a medication in which the tissue resembles lichen planus.

Liesegang rings: Histologic characteristic of the calcifying epithelial odontogenic tumor denoting calcification bodies in the amyloid-like material of the tumor.

Lingual varix: Enlarged vein under the tongue.

Lipopolysaccharides: Component of gram-negative bacterial cell walls.

Liquefactive necrosis: Cell death associated with bacterial infections and abscess formation.

Localized: Limited to a focal or small area.

Locus: Specific location of a particular gene on a chromosome.

Ludwig angina: Cellulitis involving the submaxillary, submental, and sublingual spaces.

Lumen: The space in the interior of a tubular structure.

Lupus erythematosus: A chronic autoimmune disease that may involve the skin and mucosal surfaces as well as multiple body systems.

Lymphadenopathy: Enlarged lymph nodes resulting from disease or infection of the nodes, making them palpable. The nodes feel firm and may appear larger than normal.

Lymphangioma: A congenital lesion comprising lymphatic vessels, lymph tissue, and capillary mixtures.

Lymphocyte: Mononuclear, nonphagocytic leukocyte.

Lysosomal enzyme: Strong digestive enzymes found in the lysosomes of cells.

Lysosome: Organelle that contains digestive enzymes.

Macroglossia: Abnormally enlarged tongue.

Macrophage: Large, mononuclear, phagocytic cells that are fixed in tissues.

Macrovascular: Pertaining to the larger blood vessels.

Macule: Flat lesion differentiated from the surrounding tissue by color only.

Maculopapular: A skin reaction that consists of flat colored areas and raised colored areas.

Major histocompatibility complex (MHC): Molecules on the surface of an individual's cells that identifies the cells as self.

Malignant: Neoplastic growth that has the ability to spread to distant sites by metastasis.

Mammography: Method of screening for breast cancer.

Manifestation: An observable or quantifiable characteristic associated with a specific type of pathology.

Mandibular tori: Production of excess bone in the labial and lingual area of the mandible. Stressors, genetic predisposition, and ethnicity appear to play a role in the development.

Margination: Movement of leukocytes toward the endothelial cells of a blood vessel at the site of an injury.

Mast cell: Granular cell that is located near epithelial surfaces and the surfaces of blood vessels; releases histamine.

Melanin: Refers to a pigment produced by melanocytes that is responsible for skin color.

Melanocytes: Pigment synthesizing cells that are located at or in the basal cell layer. They function to produce pigment granules called melanin.

Melanoma: A malignant growth comprising cells that produce melanin or melanocytes.

Melanosis: An abnormal brown or brown-black pigmentation of the tissue because of increased melanin within the tissues.

Membrane attack complex: End product of the complement system cascade that acts to cause lysis of foreign or targeted cells.

Memory cell: B lymphocyte that has been encoded with antigenic information so that the immune system can produce antibodies the next time it encounters the same antigen.

Metaphyseal: A conical section of bone between the epiphysis and the long bones.

Metaplasia: An adaptive change in which the normal cell type is replaced with another normal cell type.

Metastasis/metastatic/metastasize: The spread of malignant tumor cells to a distant site away from the initial or primary tumor.

Metastatic calcifications: Condition in which calcium salts accumulate in otherwise healthy tissue due to excessive levels of calcium in the blood (hypercalcemia) as might occur in hyperparathyroidism.

Microangiopathy: Small blood vessel pathology.

Microcirculation: Circulation within the small blood vessels including the arterioles, capillaries, and venules.

Microstomia: A restricted mouth opening.

Milia: Benign cysts commonly found on the skin.

Minocycline (black bone stain): A semisynthetic tetracycline derivative whose use sometimes causes pigmentation of the oral tissues, bone, and nail beds, producing what is called black bone staining.

Mitosoid figures: Cells in which the nuclear DNA has fragmented, resulting in a cell that looks like it is undergoing mitosis.

Mitotic figures: Cells that are undergoing any stage of mitosis.

Mixed: In regard to radiopacity, containing both radiopaque and radiolucent components.

Monocyte: Large mononuclear leukocyte that is found circulating in the blood.

Monosomy: Having only one chromosome instead of a pair of chromosomes.

Morbidity: A diseased or abnormal state.

Mulberry molars: Found in congenital syphilis as part of Hutchinson triad. Molars have a "mulberry" shape.

Morphogenesis: The differentiation of embryonic cells and their development into the necessary organs and structures.

Morsicatio buccarum: Scientific term for chronic cheek chewing. *Morsus* is Latin for bite.

Mortality: Death rate.

Mosaicism: Having cells that contain different genotypes within the same individual caused by a genetic mutation or chromosomal abnormality that occurs early in the development of the embryo.

Motile phagocytes: Phagocytic cells capable of independent movement.

Mucocele: Clinical term used to describe a mucosal swelling filled with mucin.

Mucositis: Inflammation of the mucosal surfaces of the mouth or digestive tract.

Mucous patches: Patches found in the secondary stage of syphilis.

Mucus extravasation phenomenon: Mucocele that is lined with granulation tissue and caused by severance of a salivary excretory duct, resulting in mucin spilling over into the surrounding tissue.

Mucus retention cyst: Mucocele that is caused by blockage of the duct usually associated with a salivary stone or sialolith.

Multifactorial inheritance: Traits and/or conditions affected by the interaction between genetic and environmental factors.

Multilocular: Having many compartments or cells.

Mutation: A change in the chemistry of a gene that is perpetuated in subsequent divisions of the cell in which it occurs; a change in the sequence of base pairs in the chromosomal molecule.

Mycobacteria: Bacteria that belong to the *Mycobacteriaceae* family, which are characteristically gram-positive, rods, and associated most

often with infections that affect people with suppressed immune systems such as tuberculosis.

Myoepithelial cells: Epithelial cells located in the salivary gland acini that contract and move saliva through the ducts of the glands.

Myxedema: Edema of the skin associated with hypothyroidism, usually seen in the face and/or shins.

Natural killer cell: Type of T lymphocyte that destroys viral infected cells and tumor cells but does not need activation to recognize antigens.

Necrosis: Pathologic death of a cell, tissue, or organ.

Necrotizing sialometaplasia: The entity originates from salivary gland ischemia caused by trauma in the local area.

Necrotizing ulcerative gingivitis (NUG): A disease that presents with necrotic gingivitis involving the interdental papillae and generalized erythema throughout the mouth.

Negative feedback system: Regulatory system that controls hormone levels by stimulating hormone release in response to an inadequate (negative) level of hormone in the body.

Neoperiostosis: Periosteal cellular proliferation with generation of new bone over the existing cortical bone that appears clinically as osseous expansion and radiographically as cortical layering; often called "onion skinning."

Neoplasia: New growth of cells.

Neoplasm: Any abnormal growth of new tissue, benign or malignant.

Nephropathy: Any one of many forms of kidney disease.

Neurohypophysis: The posterior portion of the pituitary gland.

Neuropathy: Any disease that affects the nervous system or any part thereof.

Nevus/nevi (plural): Benign localized overgrowth of melanin-forming cells of the skin present at birth or appearing in early life; commonly called a mole.

Nevoid basal cell carcinoma syndrome: Also known as Gorlin-Goltz syndrome. A key factor in the disease is the presence of odontogenic keratocysts. It is an inherited autosomal dominant disorder. The syndrome has five key components: nevoid basal cell carcinoma, jaw cysts, congenital skeletal anomalies, ectopic calcifications, and palmar and plantar pits.

Nikolsky sign: The epithelial stripping and production of a vesicle or bulla when gentle pressure is applied to skin or mucous membranes.

Nocturia: Excessive nighttime urination.

Nodule: A solid raised soft tissue growth not filled with fluid and larger than 0.5 cm but less than 2 cm.

Noncytotoxic virus: A virus that does not cause cell death and may remain dormant in an infected cell.

Nondisjunction: Failure of paired chromosomes to separate and migrate to the opposite poles during anaphase.

Nonpathogen: An organism that does not cause disease.

Nonspecific (natural or innate) immunity: Nonspecific immunity conferred by the first line defense systems of the body.

Nonvital tooth: A tooth in which the pulp is no longer living; the tooth will test negative when a pulp-testing device is used on the tooth surface.

Nosocomial: Infection or condition acquired in a hospital or long-term care facility that is related to the care given at the facility.

Nuclear hyperchromatism: Increased nuclear staining that is a cytologic feature of malignancy or premalignancy.

Odontogenic cysts: Cysts that are formed from remnants of one of the tooth-forming organs.

Odontogenic keratocyst: Very aggressive cyst that develops from the dental lamina or its remnants. Usually occurs in posterior mandibular region.

Odontogenic myxoma: Derived from the odontogenic ectomesenchyme and originates in the periodontal ligament or dental pulp. They are capable of rapid growth and are very persistent. Root absorption and displacement can occur.

Odontogenic tumor: Tumors derived from the epithelial or mesenchymal remnants of the tooth-forming apparatus.

Odontoma: A mixed odontogenic tumor of epithelial and mesenchymal tissues. They are developmental anomalies and are hamartomas.

Oligogenic inheritance: Inheritance that is related to the interaction of more than one gene located at different loci.

Oncogene: Gene that has the capability to cause a normal cell to become malignant.

Oophoritis: Inflammation of the ovary.

Opportunistic infection: An infection caused by normally nonpathogenic organisms in an immunocompromised patient.

Opsonins: Substances that enable the white blood cells to phagocytize resistant bacteria and other substances.

Opsonization: The process by which bacteria are targeted to enable phagocytosis.

Oral glucose tolerance test: Blood glucose is checked after fasting overnight and again 2 hours after drinking of a glucose-rich solution.

Orchitis: Inflammation of the testis.

Orthopnea: Difficulty breathing when in a supine position.

Oral submucosa fibrosis (OSF): A premalignant condition seen predominantly in Southeast Asia with the use of betel nut, areca nut, and tobacco products. The mucosa loses its elasticity, and dense fibrous bands cause restriction of the tissue and oral squamous cell with long-term use.

Osteoma: A benign tumor consisting of mature compact or cancellous bone.

Osteomyelitis: Chronic or acute inflammation within the bone. Caused by trauma and are composed of bacteria.

Osteopetrosis: Also referred to as Albers-Schönberg disease (see definition above).

Osteophyte: Growth of bone at the periphery of a joint.

Osteopenia: Decreased bone density or reduced bone mass.

Osteoporosis: Excessive loss of bone mass leaving the individual at risk of pathologic fractures usually in the hip or spine.

Osteosarcoma: The most common malignant tumor found in bone.

Papillary: Consisting of finger- or nipple-like projections.

Papilloma: A benign exophytic papillary growth of stratified squamous epithelium.

Papule: A small, less than 5 mm, solid raised lesion that is not fluid filled.

Paradental cyst: Cyst derived from the reduced enamel epithelium usually found at the bifurcation areas of molars, thought to be a variant of the dentigerous cyst.

Parafollicular cell: Thyroid gland cell that produces calcitonin.

Parafunctional: Not related to normal function, characterized by abnormal function.

Parakeratotic/parakeratosis: An abnormal formation of keratin cells in the stratum corneum that have retained their nuclei, may contain abnormal keratin, and contain too much water, causing swelling of the cell.

Paraneoplastic syndromes: Systemic manifestations of malignant tumors not directly related to the tumors themselves.

Parenchymal tissue: The tissue that distinguishes one organ from another.

Parotitis: Inflammation of the parotid gland.

Parosteal osteosarcoma: The primary malignant tumor found in bone. Mutations of the *Rb* gene and *p53* gene are common in these tumors.

Paroxysm: Spasm or convulsion.

Paroxysmal nocturnal dyspnea: Sudden shortness of breath that occurs during sleep without warning because of pulmonary congestion associated with left-sided heart failure.

Passive immunity: Immunity obtained from receiving preformed immunoglobulins across the placenta, from breast milk, or by injection.

Patch: A flat lesion greater than 1 cm in size that is differentiated from the surrounding tissues by its color and/or texture.

Pathogen: A disease-causing organism.

Pathogenesis: The sequence of events that occur in the development of a disease or condition.

Pathognomonic: Denoting one or more typical symptoms, findings, or pattern of abnormalities that allows nearly instant recognition of a disease.

Pathologic murmur: Abnormal heart sounds caused by a heart defect or acquired damage.

Pathology: The study of disease or abnormal conditions.

Pavementing: Process in which leukocytes "stick" to the walls of the blood vessels before emigration through the endothelium; also known as adhesion.

Pedunculated: A growth attached to the surface of the tissue by a stalk that is thinner than the base of the growth.

Penetrance: Refers to the number of individuals who possess a particular genotype and exhibit the characteristics of that genotype in their phenotype.

Percussion: Striking a tooth with short, sharp blows as a diagnostic tool in an attempt to elicit pain.

Periapical granuloma: Also referred to as dental granuloma or apical periodontitis. This is the result of necrotic pulp tissue and the inflammatory process damaging the tissues adjacent to root of the tooth.

Perineural invasion: Extension of neoplastic cells into the cells that surround and support the nerves of the peripheral nervous system.

Perioral skin: The areas of tissue that surround the mouth to include the nasal labial area, the mouth, and the chin.

Periosteal: A term that relates to the periosteum or the thick fibrous membrane covering the entire surface of a bone.

Periosteum: Connective tissue membrane covering the surfaces of bones.

Peripheral neuropathy: Any disorder that affects the nerves in the periphery of the body (i.e., arms and legs).

Peripheral giant cell granuloma (giant cell epulis): A reactive hyperplastic response to tissue injury producing an exuberant growth of tissue in the area of injury.

Peristalsis: The reflexive movement of muscles in a tubular structure that move a substance through the structure.

Peritoneal cavity: Abdominal cavity.

Perineural invasion: Surrounding and invading a nerve.

Perlèche: Another name for angular cheilitis or infection of the commissures of the mouth by a candida infection.

Permanent cells: Cells that do not replicate when mature.

Permeable: Permitting passage of a substance.

Pernicious anemia: An autoimmune disorder that inhibits the formation of intrinsic factor and thereby interferes with the transportation of vitamin B_{12} across the gastrointestinal mucosa causing a megaloblastic type of anemia.

Petechiae: Any tiny, perfectly round, purple to red spot that appears on the skin because of minute intradermal or submucous hemorrhage. The spots are small, ranging from 1 to 2 mm and may be associated with certain disease states.

PFAPA syndrome: A syndrome that involves periodic fever, aphthous stomatitis, pharyngitis, and adenitis found in early childhood.

Phagocyte: A cell possessing the ability to ingest bacteria, foreign matter, and other cells.

Phagocytosis: The process of ingestion and digestion by cells of solid substances such as bacteria and bits of foreign matter.

Phagosome: Vacuole that is formed when a phagocytic cell engulfs foreign matter.

Phenotype: How an individual's genotype is exhibited to others, what the individual looks like, etc.

Philadelphia chromosome: An abnormal chromosome formed by the translocation of pieces of chromosome 9 and 22.

Phlebolith: A calcified deposit in a venous wall.

Phlebotomy: Bloodletting.

Photophobia: Fear of, or sensitivity to, light that results in eye pain or discomfort.

Physiologic murmur: Abnormal heart sounds made by a normally functioning heart.

Physiologic pigmentation: Normal pigmentation caused by increased melanin production and not by increased numbers of melanocytes.

Pindborg tumor: Another name for calcifying epithelial odontogenic tumor.

Plaque: A raised lesion with a broad flat top that looks pasted on.

Plasma cell gingivitis: A term associated with allergic responses to certain substances such as preservatives, additives, and products.

Plasma cells: B lymphocytes involved in the synthesis, storage, and release of antibodies.

Plasma fluid: The fluid portion of the blood.

Platelet-activating factor: Chemical mediator that causes the aggregation of platelets.

Pleomorphism: Cells that present with different sizes and shapes of the same cell type.

Pleural cavity: The space in the chest that houses the lungs.

Plumbism: Lead poisoning.

Pluripotential stem cell: A cell that has the ability to develop into numerous types of blood cells including erythrocytes, platelets, and lymphocytes.

Polycythemia: An abnormal increase in the number of red blood cells.

Polydipsia: Excessive thirst of a chronic nature.

Polymorphism: Normal variations associated with a specific gene.

Polymorphonuclear neutrophils: A type of leukocyte having nuclei of varied forms.

Polyp: Mass of tissue that projects out from the surface level of a structure.

Polyphagia: Excessive hunger.

Polyposis: The presence of several polyps. Adenomatous coli or familial adenomatous is a term used in relation to the presence of malignant polyp development in Gardner syndrome.

Polyuria: Excessive urination caused by one or more of several diseases of a chronic nature.

Prayer sign: Inability to press the palms of the hands and fingers firmly together.

"Precystic" epithelial proliferation: Initial stage of cyst development whereby the epithelial remnants (rests) of the tooth development organs are stimulated and begin to grow (proliferate), eventually forming a walled off, fluid-filled, lumen (cyst).

Prediabetes: A blood glucose level that is higher than normal but not high enough to be considered diabetes; also known as impaired glucose tolerance.

Premalignant lesion: A specific clinical alteration in tissue that predisposes to a high likelihood of malignant transformation.

Primary immune response: Immune response that occurs on the first exposure to an antigen.

Primary immunodeficiency: Congenital or inherited abnormalities in the immune system that cause it to function less efficiently.

Primary tumor: Original site of tumor formation from which other tumors have spread through the body.

Primordial cyst: A variant of the odontogenic keratocyst that technically develops in place of the existing tooth or before any calcification of the tooth.

Prodrome: Symptom preceding the onset of a disease. Often presents as tingling, burning, or pruritus.

Prognathism: Protrusion of the mandible or maxilla past its normal relationship with the opposite arch.

Prognosis: A statement regarding the likely outcome of a disease or condition.

Proliferation: Growth or reproduction of cells of the same sort.

Proliferative verrucous leukoplakia: An aggressive form of leukoplakia that has a high likelihood of malignant transformation and degeneration.

Prophylactic: Tending to ward off or prevent a disease process or condition from occurring.

Proprioceptive: The feeling of body movement and position sensed by the nerves of the musculoskeletal system and the inner ear.

Prostaglandin: Chemical mediator produced by leukocytes that causes vasodilation, increased vessel permeability, and increased feelings of pain.

Proto-oncogene: Normal gene that plays a part in the growth and replication of cells.

Pruritic: Abnormal sensation in the skin; also called itchy.

Pruritus: Denotes an itching of varying intensity.

Pseudoanodontia: Early exfoliation or delayed eruption of primary and permanent teeth that results in the clinical appearance of missing teeth.

Pseudocysts: Lesions that have an accumulation of fluid in a cyst-like structure but do not have an epithelial lining.

Pseudomembrane: A false membrane comprising debris and necrotic tissue covering a mucosal ulcer or other lesion that can be wiped off.

Psychogenic: Having a mental or psychological etiology.

Pulmonary hypertension: Abnormally high blood pressure within the pulmonary circulation.

Punch biopsy: Method of obtaining cells for microscopic examination that removes a cylindrical core of tissue from the suspect area using a large needle or other such instrument.

Purpura: Circumscribed hemorrhagic lesions that measure from 0.1 to 5.0 cm in diameter in the skin or mucous membrane surface.

Purulent exudate: Pus.

Pustule: Vesicle filled with pus instead of clear fluid.

Pyknotic: A degenerative state of the cell nucleus.

Pyogenic: Pus forming.

Pyogenic granuloma: An exuberant connective tissue proliferation produced as a reaction to a stimulus or to an injury.

Pyrexia: Fever.

Pyrogen: Agent (i.e., chemical/organism) able to produce a fever.

Quid: A confined packet made of a betel leaf with products usually consisting of areca nut, slaked lime, flavoring agents and tobacco products that are placed inside the leaf that is folded or rolled.

Radiation caries: Caries that occur as a result of the acidogenic actions of cariogenic bacteria in the presence of xerostomia caused by permanent radiation damage to the salivary glands.

Radicular cyst: A cyst that is always associated with the root of a nonvital tooth. Common causes are caries, trauma, or periodontal disease.

Radicular: Pertaining to the root of a tooth.

Radiolucent: A radiographically darker appearing area.

Radiopaque: A radiographically lighter or whiter appearing area.

Radiosensitive: Acutely affected by ionizing radiation.

Ramsay Hunt syndrome: The facial nerve is affected in a disease process such as herpes zoster resulting in facial paralysis, diminished hearing, and vertigo.

Raynaud phenomenon: Characterized by numbness and pallor of the fingers, toes, and nose because of intermittent lack of blood flow to the fingers.

Recalcitrant: Markedly resistant to a form of therapy.

Recessive: Genes that require a pair of homozygous alleles for the trait to be expressed in the phenotype of an individual; a recessive gene will not be expressed when paired with a dominant heterozygote allele.

Regeneration: Reproduction of a lost or injured part.

Regurgitate: Back flow of blood.

Reiter syndrome: A syndrome that is caused by a venereal disease or dysentery producing a triad of urethritis, conjunctivitis, and arthritis.

Relapse: Recurrence of the signs and symptoms of a disease or condition after a period of normalcy.

Rendu-Osler-Weber disease: Another name for hereditary hemorrhagic telangiectasia.

Repair: Restoration of diseased or damaged tissue by healing or surgery.

Reservoir: Substance or living host within which an organism can multiply and develop and potentially be transmitted to a susceptible host.

Residual cysts: Cysts that develop after the stimulating inflammatory products have been removed from a previous cyst. Some by-products may have remained and stimulate the development of a new cyst.

Resistance: The ability of the host to defend itself against pathologic organisms, toxins, and other harmful agents.

Resolution: Return to normal.

Resorption: A physiologic or pathologic removal of bone substance.

Rests of Malassez: Epithelial remains of Hertwig root sheath in the periodontal ligament.

Rests of Serres: Odontogenic rests with remnants of the dental lamina that originate from the connection between the mucosa and the enamel organ.

Retinopathy: A degenerative disorder of the retina.

Retromolar trigone: The soft tissue area posterior to the mandibular molars that extends toward the pharynx.

Retrovirus: A virus with a central core of RNA as opposed to DNA.

Reverse smoking: Method of smoking tobacco in which the lit end is placed in the mouth when the smoke is inhaled.

Risk factor: A contributing or predisposing element leaving an individual with a higher probability of having a condition or having an exacerbation of a condition.

Rosacea: A chronic vascular and follicular dilation involving the nose and cheeks.

Sarcoidosis: A systemic disease affecting multiple organs, skin, eyes, and especially targeting the lungs, exhibiting interstitial fibrosis.

Sarcoma: Cancer of tissues arising from the mesoderm (i.e., connective tissue, muscle, or bone).

Sclerodactyly: The thickening or hardening of the skin of the fingers and toes associated with scleroderma.

Scleroderma: An immune dysfunction that is characterized by fibrosis of the skin, organs, and collagen. Several disease states are associated with scleroderma such as Sjögren syndrome, Raynaud phenomenon, and rheumatoid arthritis.

Seborrheic keratosis: Overproduction of sebum by the sebaceous glands causing an overproduction of the horny layer of the skin.

Secondary immune deficiency: An immune deficiency that is acquired later in life and may be the result of infection, malignancies, immunosuppressant drug therapy, or other causes.

Secondary immune response: Immune response that occurs on second and subsequent exposures to an antigen.

Seeding: The spread of cancer by cells that have broken off from an established tumor and traveled through the peritoneal or pleural cavities to establish a metastatic tumor in an adjacent organ.

Self-tolerance: Ability of a body's cells to recognize its own cells.

Septicemia: Systemic disease caused by microorganisms in the circulating blood.

Sequela: A condition resulting from another pathologic condition.

Sequestrum: Refers to a fragment of necrotic bone that has broken away from the healthy tissue in the surrounding area.

Seroconversion: Point in time at which antibody to HIV is detectable in the blood of an infected individual.

Seropositive: Having antibodies to HIV in the blood denoting the presence of the disease.

Serotonin: A chemical mediator.

Serous exudate: Thin, watery fluid leaking from cells into tissues.

Sessile: A growth attached to underlying tissue by a base as broad as the lesion itself.

Shunt: An abnormality that diverts blood from one area of the heart to another.

Sialolith: A salivary stone, and sometimes ductal scar tissue causing obstruction of the involved salivary gland.

Sign: An objective observation of a disease element such as findings from laboratory tests and physical examination.

Simian crease: A single transverse crease across the palm of the hand seen in several genetic disorders including trisomy 21.

Smoker's melanosis or smoking-associated melanosis: Irregular, hyperpigmented macules usually associated with smoking tobacco products, especially prevalent in female smokers. They are usually prominent in the maxillary anterior labial gingival, buccal mucosa, and soft palate.

Solar lentigo: See "Lentigo".

Somatic: Anything relating to all of the cells of an organism excluding the gametes or sex cells.

Specific immunity: See "Acquired immunity".

Speckled leukoplakia: Nonhomogeneous form of leukoplakia characterized by small whitish nodular elevations with an erythematous base, which are strongly associated with potential malignancy.

Spongiosis: Inflammatory intercellular edema of the epidermis.

Squamous cell carcinoma: A type of malignant neoplasm derived from epithelial cells and chiefly from squamous cells.

Stable (quiescent) cells: Cells that will undergo replication only if needed to repair or restore function of the organ or tissue.

Static bone cyst: Also known as Stafne bone cyst. This bone cyst is not a true bone cyst. It results from a defect in the mandible that surrounds salivary gland tissue. It is believed to be an entrapment of salivary gland tissue and it is not lined with epithelium.

Stellate reticulum: One of the layers of the developing enamel organ. It must be present for the formation of enamel to progress.

Stomatitis medicamentosa: An allergic reaction of the oral mucosa to the systemic administration of a medication.

Stomatitis venenata: An allergic response to an agent such as dental products or food products that produce an inflammation in the mouth.

Stress: Reaction of the body to external or internal stimuli that initiates a protective response within the body.

Striae: A band, streak, or stripe of skin that is a different color, texture, or elevation from the surrounding area.

Subclinical infection: Infection in which the host does not develop clinically observable signs of disease.

Submucous fibrosis: A premalignant condition of the oral mucosa resulting from the use of tobacco, areca nut, or betel quid characterized by leathery appearance, pigmentation, palpable fibrous bands, and key histologic features.

Subpontic osseous proliferation: Bony growths that develop under a posterior bridge pontic.

Susceptibility: The probability an organism will be affected by an external stimulus or other organism.

Sutton disease: Another term sometimes used for major aphthous ulcers.

Symblepharon: Adhesion of the inner eyelid tissue to the eyeball. This is a characteristic found in mucous membrane pemphigoid.

Symptom: Subjective report of the patient indicating a disease or pathologic condition.

Syndrome: A group of signs or symptoms that occur together and are associated with a disease.

Syphilis: A venereal disease caused by the spirochete *Treponema pallidum*.

Target cell: A cell that has receptors for specific hormones or substances located on its cell membrane.

T-cytotoxic cell: T lymphocyte that has the ability to destroy cells that it has been activated against.

Telomere: The end piece or cap of a chromatid.

Tensile strength: The resistance of a material to a force tending to tear it apart; the ability of a material to deform and return to normal without breaking or tearing.

Teratogen: Any chemical, environmental, or biological agent that can cause congenital malformations.

Teratology: The study of developmental anomalies in embryos or fetuses.

Teratoid cyst: Cyst compiled of misshaped or misplaced parts, a combination of forms.

Teratoma: A developmental neoplasm comprising tissues from all of the embryonic germ layers.

Tetany: Muscle spasms and twitches caused by low blood levels of calcium or magnesium.

Tetraploid: A cell containing four sets of chromosomes.

T-helper cell: T lymphocytes that enhance the response of other B and T cells.

Thrill: A vibrating or pulsating sensation, such as the pulsating of an artery.

Thrombocytopenia: A decrease in the number of platelets causing clotting deficiencies.

Thrombus/thrombi (plural): A blood clot or clots that are attached to the intima of a blood vessel.

Thyroid storm: A life-threatening emergency caused by a sudden worsening of symptoms in a person who has preexisting hyperthyroidism.

Tonsilloliths: A concretion (calcification or stone) in a tonsil crypt.

Tori: Exuberant production of bone in both the maxillary and mandibular regions.

Torus palatinus: Exuberance of bone forming in the palatal region of the mouth.

Trait: A distinct phenotypic characteristic that can be separated from other characteristics.

Transient ischemic attack (TIA): Temporary reduction of blood flow to a part of the brain causing reversible stroke-like symptoms, often a warning sign for CVA.

Translocation: The rearrangement or movement of segments of one chromosome to another.

Transmigration: Movement across a barrier, a term sometimes used instead of emigration.

Traumatic ulcer: A term used to describe an injury to the tissue resulting in a crater with an area of denuded epithelium.

Traumatic bone cyst: Also called a simple bone cyst, associated with trauma.

Triploid: A cell containing three sets of chromosomes.

Trismus: Spasms or continuous contraction of the masseter muscle.

Trisomy: Condition in which there are three sets of any one chromosome, as in trisomy 21.

Troche: Medication in lozenge form.

Tumor: A large, greater than 2 cm, elevated lesion that is not fluid filled.

Tumor necrosis factor: Chemical mediator.

Tumor staging: A system of classifying a tumor as to potential therapies and outcomes based on the size of the tumor, extent of lymph node involvement, and presence of metastasis.

Tumor suppressor gene: Gene that plays a part in inhibiting uncontrolled growth of cells.

Tzanck cells: Free-floating epithelial cells caused by acantholysis (loss of cohesiveness between the cells). Tzanck cells are histologically diagnostic for pemphigus vulgaris when there is separation of the epithelial tissue.

Ulcer: A depressed lesion that penetrates both the epithelium and the lamina propria and has lost the epithelial covering of tissue.

Unilocular: Consisting of a single compartment.

Unstable angina: Category of angina that presents with angina symptoms not associated with any exertion or stress.

Urticaria (hives): Pruritic wheals caused by a hypersensitivity reaction

Vacuolated: Clearing of the cytoplasm of a cell.

Varix (varicosity): A dilated vein.

Vascular stasis: Slowing of the blood through the vessels.

Vasoconstriction: A decrease in the diameter of blood vessels.

Vasodilation: An increase in the diameter of blood vessels.

Venereal disease (sexually transmitted disease): Infection caused or propagated by sexual contact.

Venous varix: An enlarged vein often found on the lip.

Ventricular fibrillation: Rapid disorganized ventricular contractions that take the place of normal contractions and fail to move blood effectively through the heart.

Verrucous leukoplakia: Nonhomogeneous form of leukoplakia characterized by irregularity of the surface.

Vesicle: A small, less than 0.5 cm, elevated lesion filled with a clear liquid.

Vesiculobullous: Diseases characterized by fluid-filled blisters.

Violaceous: Denotes a purple discoloration. This term is used in the description of lichen planus.

Viral load: The plasma level of viral RNA in the peripheral blood.

Vitiligo: An autoimmune response causing the loss of melanocytes in certain skin areas. The skin surface becomes devoid of pigmentation and appears white in color.

Waldeyer ring: Ring of oropharyngeal lymph tissue comprising the lingual and palatine tonsils and the pharyngeal tonsil or adenoid.

Warts (verrucous vulgaris): A wart produced by various types of the human papilloma virus. The surface will vary depending upon the location and the strain of the virus. The warts are usually removed by freezing, burning, or by various acids.

Wickham striae: Interlacing white lines characteristic of lichen planus.

Xanthelasma: Characterized by yellow plaques that are especially noticeable when located on the eyelids and below the eye at the medial canthus. The papules have been associated with hyperlipidemia and with low-density lipoproteins.

Xerophthalmia: Dry eyes or keratoconjunctivitis sicca.

Xerostomia: Inadequate salivary flow or problems with the consistency or composition of saliva produced.

X-linked: A trait that is carried on the X (female) chromosome.

Xylitol: A five-carbon sugar alcohol used as a sugar substitute.

Zygote: The diploid cell created when the egg is fertilized by the sperm and the cell mass that represents the very early developmental stage of the embryo.

INDEX

Note: Page numbers in *italics* denotes figures and those followed by "t" denotes tables and those followed by "b" denotes boxes.

A

ABCDE rule, 105b–106b
Abdominal aortic aneurysm (AAA), 203–205, *204*
Abfraction, 278, 551
Ablated lesions, 400
Abrasions, 12, 551–552, *552*
Abscess, 55–56, *56*
Abuse and neglect, 23t
Acanthosis, 396
Acanthosis nigricans, 185, *185*
Accessory teeth, 559–560, *560*
Acinic cell carcinoma, 466–467, *467*
Acquired immunity
  active immunity, 70–71
  cellular and chemical components, 66, 67t
  immune response
    cell-mediated immunity, *69,* 69–70, *70*
    humoral immunity, 66–69, *67, 68,* 68b
  organs associated with, 66
  passive immunity, 71
Acrochordon, 613–614, *614*
Acromegaly, 89, 164–165, *165*
Actinic cheilitis, 613, *614*
Actinic keratosis, *613*
  basal cell carcinoma, 101, 102
  locations, 613
  white lesions, 398, *398*
  treatment for, 613
Actinomycosis, 338-339, *339*
Active immunity, 70–71
Acute adrenal insufficiency, 75
Acute inflammation
  cardinal signs, 46, 46t
  outcomes of, 53, *53*
    abscess formation, 55–56, *56*
    chronic inflammation, 53–55, *55,* 55b
    fibrous repair (*see* Fibrous repair)
    inflammatory process resolution, 56
    regeneration, 56
    tooth extraction, 60, *60*
  phases of
    amplification phase, *47,* 48, *49*
    initiation phase, *47,* 48, *49*
    termination phase, 48, 50
Acute lymphonodular pharyngitis, 317
Acute necrotizing periodontitis, *598,* 598–599
Acute pseudomembranous candidiasis, 392–393, *393*
Adaptive cellular changes, *35*
  atrophy, 35, *35*
  dysplasia, 37, *38*
  hyperplasia, 36, *37*
  hypertrophy, 35–36, *36*
  intracellular substances retention, 38, *38, 39*
  metaplasia, 36–37, *37*
  neoplasia, 37–38
  oxygen deprivation, 34–35
Adenocarcinoma, 353
Adenohypophysis, 161
Adenoid cystic carcinoma, 468, *468*
Adenomatoid odontogenic tumor, 533–538, *537*
Adenomatous polyps, 109
Adhesion, *47,* 48, *49*
Adjuvant therapy, 466
Adrenal gland disorders
  acute adrenal insufficiency, 173
  adrenocortical insufficiency, 170, 172, *172*
  hyperadrenalism, 173–174
Adrenocortical insufficiency, 172–173, *172*
Advanced glycation end products (AGE), 176
Agenesis, 118
Agent-induced osteonecrosis of the jaw (ARONJ), 287
Agranulocytes, 50–51, *51,* 51b
AIDS (*see* Human immunodeficiency virus (HIV) infection)
AJCC Cancer Staging Manual Anatomic Stage/Prognostic Groups, 95, 96t
Albers-Schönberg disease, 511
Allergic contact dermatitis (ACD), *76,* 76–77, *77*
Alopecia, 99
Alternative pathway, 52
Alveolar osteitis, 60
Amalgam tattoo, 14, *14,* 413, *414*
Amelanotic melanoma, 426
Ameloblastic fibroma, 538-539
Ameloblastoma, 489
Amelogenesis imperfecta
  enamel development stages, 572
  enamel structure loss, 573
  hypocalcified forms, 572
  hypomaturation type, 572
  radiographic pattern, 573
  treatment, 573
Anaphylactic reactions, 72–73, 73b
Anaplastic changes, *95*
Anemia, 97, 99
  aplastic anemia, 237, 237b
  chronic diseases, 237, 237t
  definition, 229
  hypochromic (iron deficiency) anemia, 229–231, 230t, *231*
  megaloblastic, 233–235, *234*
  sickle cell disease, 235–236, 236t, *236*
  thalassemia, 231–233, *231, 232*
Aneuploid cells, 131
Aneurysm, 198
Aneurysmal bone cyst, 522–523
Angina, 201
Angioedema (AE), *73,* 73–74
Angiogenesis, 57
Angular cheilitis
  HIV and AIDS, 593, *594,* 616, *616*
  red and purple lesions, 373, *373*
Angular stomatitis, 616, *616*
Ankylosis, 506
Anodontia, 147
  complete, 557
  false, 558
  hereditary hypohidrotic ectodermal dysplasia, 558–559, *559*
  incontinentia pigmenti, 559
  partial, 557, *558*
  pseudoanodontia, 558
  true, 557–558
Anorexia, 97
Antiangiogenesis therapy, 98
Antibodies, 66, 68–69, 68b
Antigen-binding fragment (Fab), 66
Antigen-presenting cell (APC), 69
Antigens, 65
Antihormone therapy, 98
Antithrombotic therapy, 202b
Aphthous ulcers, 341–344, *342–343*
Apical periodontal cyst (*see* Radicular cyst)
Aplastic anemia, 237, 237b
Apoptosis, 40, *40*
Apoptosis regulating genes, 91
Argyria, 415
Arteritis, 210
Asthma, 75, 269b, 269–270
Ataxia, 233
Atelectasis, 268
Atherosclerosis, 197–199, *198*
Atopic reactions, *73,* 73–74, 388
Atrial septal defect (ASD), 210
Atrophic candidiasis, 593, *594*
Atrophy, 35, *35*
Attrition, 550–551, *551*
Autoimmune disease, 77–78, *78,* 78t
Autoimmune thyroiditis, 166
Autoinoculation, 435

Autonomic neuropathy, 178, 201
Autosomal chromosomes, 125
Autosomal dominant disorders, 136, *136,* 138b
Autosomal dominant genetic inheritance, 560
Autosomal recessive disorders, *136,* 137, 138b
Azidothymidine (AZT) associated pigmentation, 417, *417*

B

Bacteremia, 55
Bacterial sialadenitis, 457
Balloon angioplasty, 203, *203*
Barr body, 126, *127*
Basal cell carcinoma (BCC), 100–101, *101,* 102, 610
Basal keratinocytes, 411
Basal metabolic rate (BMR), 168
Basophils, 50, *50*
Behçet syndrome, 344–345
Bell palsy, 279–280, 279b, *280*
Benign chondroma, *89*
Benign migratory glossitis, 388, *388*
Benign neoplasms
  brain tumor, 89
  clinical characteristics, 87, 88t
  endocrine gland tumors, 89
  histology, 89, *89*
  vs. malignant neoplasms, 88t
  nomenclature, 90t
Benign nevus, 103, 105
Benign skin lesions
  acrochordon, 613–614, *614*
  comedones, 614, *614*
  eczema, 614–615, *615*
  ephelides, 615
  keloids, 615, *615*
  milia, 615, *616*
  nevi, 615–616, *616*
  perlèche, 616, *616*
  pityriasis, 616, *616*
  poison oak, 616, *617*
  psoriasis, 617, *617*
  rhinophyma, 617, *617*
  rosacea, 617, *617*
  seborrheic keratoses, 618, *618*
  solar lentigo spots, 615, *615*
  urticaria, 618, *618*
  xanthelasma, 618, *618*
Berry aneurysm, 206, *206*
Betel quid use, 418, 419b, 420, 420b, *421*
Bilateral mandibular distomolars, 560, *561*
Bilirubin retention, 38, *38*
Biomarkers, 94
Biopsy, 20
Bismuth, 415–416
Black bone staining (*see* Minocycline tissue staining)
Black macules, 14, *14*
Blastic cells overgrowth, 243
Bleeding disorders, 248–251, 249t, *250*
Blistering and scarring, epidermolysis bullosa, *324*
Bloch-Sulzberger disease, 559
Blood diseases
  red blood cells
    anemia (*see* Anemia)
    polycythemia, 237–238, *238*
  white blood cells
    lymphoma (*see* Lymphoma)
    neutropenia (*see* Neutropenia)
Blue lesions, 14, *14*
Blue nevus, 14, *15,* 420–421, *422*
Bohn nodules, 530
Bone expansion, 19, *19*
Bone marrow suppression, 99
Bony scar, 505
Bossing, 140
Botryoid odontogenic cyst, 527 (*see also* Lateral periodontal cyst)
Bradykinesia, 278
Bradykinin, 52
Breast cancer, 107–108, 107b
Brown lesions, 14
Brush biopsy, 94, *94*
Bulla, 12, *12*
Bullous pemphigoid, 322, *322*
Burkitt lymphoma, 242–243, *243*
Burn Index, 610
Burning mouth syndrome (BMS), 282, 282b

C

Café au lait macule, 289, *290,* 469, *469*
Calcifying epithelial odontogenic tumor (CEOT), 489–491, *490*
Calcifying odontogenic cyst, 531–533
Callus, 388
Cancer grading, 95
Candidiasis
  acute pseudomembranous, 392–393, *393*
  chronic hyperplastic, 393–394, *394,* 593, *593*
  HIV infection
    angular cheilitis, 593, *594*
    atrophic candidiasis, 593, *594*
    hyperplastic candidiasis, 593, *593*
    pseudomembranous candidiasis, 593, *593*
  red/purple lesions, *372,* 372b, 371–374, *373*
Carcinoembryonic antigen (CEA), 94
Carcinogenesis
  apoptosis regulating genes, 91
  DNA repair genes, 91
  proto-oncogene, 90
  tumor-suppressor genes, 90
Carcinoma, 89
Carcinoma in situ, 91, 399, *399*
Cardiovascular system
  circulatory systems, 194
  heart, 194, *195*
  vessels, 194–195, *196*
Carditis, 215
Carotenemia, 38, *38*
Carriers, 128
Caseous necrosis, 40–41, *41,* 520
Cavernous hemangioma, 377, *378*
Celiac disease, *276,* 276–277
Cell-mediated immunity
  macrophages, *69,* 69–70, *70*
  natural killer cells, 69
  T lymphocytes, 69
Cell-mediated reactions, *76,* 76–77, *77*
Cellular adaptation (*see* Adaptive cellular changes)
Cellular injury, 41, *42*
  irreversible
    apoptosis, 40, *40*
    necrosis, 40–41, *41*
  reversible
    free radical injury, 38–39
    hypoxic cell injury, 39–40, *40*
    intracellular calcium imbalance, *40*
Cellulitis, 55, *56*
Cementoblastoma, 506–508, *507*
Cementoosseous dysplasia, 524–525
Central giant cell granuloma (CGCG), 492–493, *494*
Centromere, 124
Cerebral vascular accident (*see* Stroke)
Cervical lymphoepithelial cyst, 472–473, *473*
Chancre, 335, *336*
Cheek chewing, *389,* 389–390
Chemical and thermal burns, 391–392, *392*
Chemical carcinogenic (cancer causing) agents, 91b
Chemical mediators, *47,* 48
Chemocaries, 99
Chemokines, 52
Chemotaxis, *47,* 48
Chemotherapy, 98
Cherubism, 290, *290, 291*
Chickenpox, 312–314, *313*
Chondroma, benign, *89*
Chondrosarcoma, *89,* 495–497
Choristoma, 448
Chromatid, 124, *126*
Chromatin, 124
Chronic inflammation
  factors affecting, 55b
  granulomatous inflammation, 55, *55*
  lymphocytes, 54
  macrophages, 53–54
  tissue destruction, 54–55
Chronic morsicatio buccarum, 390
Chronic myelogenous leukemia, 90
Chronic obstructive pulmonary disease, 270–271
Chronic osteomyelitis with proliferative periostitis, 488
Cicatrix, 56
Cinnamic aldehyde allergy, 370, *371*
Circumscribed lesions, 10, *11*
Civatte bodies, 369
Classic pathway, 52
Cleft lip and palate, 148–149, 150t, 151
Cleidocranial dysplasia (CCD), 140–142, *141,* 560–561, *562*
Clinical evaluation
  diagnosis
    definitive diagnosis, 20, 25
    differential diagnosis, 19–20
    family violence, 22–25
  extraoral examinations, 4–5
    ears and skin assessment, 6
    eyes and pupils observation, 6, *6*
    follow-up questions, 6
    head and neck examination, 6, *6, 7*
    lymph nodes, 6, *7*
    physical status, 6
    temporomandibular joint examination, 7, *8*
    thyroid gland examination, 7, *8*
    upper eyelid, 6, *7*
  intraoral examination, 4–5, 7–8

buccal mucosa, 9, *9*
floor of the mouth, 9, *9*
oropharynx, 8–9, *9*
parafunctional habits, 9
saliva quality, 9
tongue, 9, *9*
objectives, 5, 6b
oral cancer screening, 5
patient record
consistency, 14–16, *15, 16*
history, 10
lesion color, 12–14
lesion distribution and definition, *10,* 10–11, *11*
lesion location, 10
lesion size and shape, 11–12, *11–12*
observations, 9–10, 10b
radiographic findings
bone expansion, 19, *19*
cortical bone destruction, 19, *19*
divergence, *18,* 19
lesion distribution, 16
lesion location and size, 16
mixed lesion, 16, *17*
multilocular radiopaque, 17, *17*
patient history, 16
periodontal ligament space widening, 19, *19*
poorly-defined margins, 17–18, *18*
radiolucent, 16, *17*
radiopaque, 16, *17,* 20
root resorption, 18, *18*
unilocular radiopaque, 17
well-defined margins, 17, *18*
Clotting system, 52
Coagulative necrosis, 41, *41*, 392, *392*
Coalescing lesions, 10, *11*
Coarctation of the aorta (COA), 211
Codominance, 128
Colloid, 165
Colobomas, 568
Colonoscopy, 94
Colorectal cancer, 109–110
Colostomy, 110
Comedones, 614, *614*
Community-acquired pneumonia, 265
Complement system, 52
Complementary therapies, 98, 98b
Complex odontoma, 508
Complication, 34
Compound nevus, 420
Compound odontoma, 508
Concrescence, 569, *571*
Condensing osteitis (*see* Focal sclerosing osteomyelitis)
Condyloma acuminatum, 437–438, *437*, *438*
Condylomata lata, 336
Congenital disorders, 118, 511–512
heart (*see* Congenital heart defects)
pigmented lesions
nevus, 420–422, *422*
oral melanotic macule, 422–423, *423*
radiopaque lesions, 511–512
soft tissue enlargements
lymphangioma, *471,* 471–472, *472*
multiple endocrine neoplasia syndrome, type 2B, 470–471, *471*
neurofibromatosis, type 2B, *469,* 469–470
syphilis, 122, *123,* 336, 336b
vesicular lesions (*see* Epidermolysis bullosa)
white lesions, 396, *396*
Congenital erythropoietic porphyria, *581,* 581–582
Congenital heart defects
dental implications, 212–213, 212b
epidemiology, 208–209
etiology, 208, 209b
extraoral characteristics
atrial septal defect, 210
coarctation of the aorta, 211
patent ductus arteriosus, 210, *210*
pulmonary stenosis, 210, *210*
tetralogy of Fallot, *210,* 210–211
transposition of the great arteries, 211, *211*
ventricular septal defect, *209,* 209–210
pathogenesis, 209
perioral and intraoral characteristics, 211
transmission method, 208
treatment and prognosis, 213
Congenital syphilis, 122, *123,* 336, 336b
Congestive heart failure (CHF), 201, 216–218, *217*
Convergence, 18
Coronal pulp chamber, 555
Coronary heart disease (CHD), 201–203, 202b, *203*
Corrugated lesion, 15, *15*
Cortical bone destruction, 19, *19*
Cowden syndrome, 451
Coxsackievirus infections, 309
acute lymphonodular pharyngitis, 317
hand-foot-and-mouth disease, 315–317, *316*
herpangina, 317, *317*
CREST syndrome, 622
Crohn disease, 274–275, 351–352, *352, 353*
Crusted lesion, 16
Cryptococcosis, 598
Cushing syndrome (*see* Hyperadrenalism)
Cusp of Carabelli, 564
Cyclic neutropenia, 145
Cyst, 518
Cystic fibrosis, *271*, 271–272
Cystic hygroma, 471, *471*
Cytokines, 52, 66, 67t
Cytotoxic reactions, 75

D

Deep fungal infections, *339,* 340–341, 340b, *341*
Delayed hypersensitivity reactions, *76,* 76–77, *77*
Demyelination, 279
Dens evaginatus, 565, *565*
Dental erosion, 169
Dental granuloma, 519
Dental hygienist's role, 4
Dental neglect, *24*
Dentigerous cyst, 528, *529*
Dentin, 551
Denture-induced fibrous hyperplasia, 450, *450*
Deoxyribonucleic acid (DNA), 86
Depapillated lesions, 388
Dermatitis herpetiformis, 276, *276*
Dermoid cysts, 474, *474*
Desmoid tumor, 459
Desquamative gingivitis, 320
Developmental abnormalities
embryo, 118
fetal alcohol spectrum defects, 120–122, *121*
fetus, 118
and inherited oral disorders, 119t
morphogenetic errors
agenesis, 118
division failure, 119
dysraphic abnormality, 118
dystopia, 119
ectopia, 119
involution failure, 118
teratogenic agents, 118, 119t, *120*
teratology, 118
TORCH syndrome, 122–123, *123*
Diabetes mellitus, 174
diagnostic tests, 176
gestational diabetes mellitus, 176, 186
prediabetes, 185
type 1 diabetes, 176–183
type 2 diabetes, 183–185
types and subclassifications, 175t
Diabetic dermopathy, 178
DiGeorge syndrome, 79
Diploid cells, 125
Discoid lupus oral lesion, 351, *351*
Disease
definition, 3
oral health and reports, 3–4, 4b
Divergence, *18,* 19
Diverticula, 272
Division failure, 119
DNA repair genes, 86, 91
Doak's cusp, 565, *565*
Down syndrome (*see* Trisomy 21)
Draining fistula, mandible, *339*
Droplet nuclei, 267
Dyskinesias, 279
Dysostosis, 560–561, *562*
Dysphagia, 94, 272–273, 368
Dysplasia, 37, *38*
Dysraphic abnormality, 118
Dysrhythmias, 210
Dystopia, 119

E

Ecchymoses, 365–367, *366*
Ectodermal dysplasia (ED), 147–148
Ectopia, 119
Eczema, 102, 614–615, *615*
Edema, 48
Ehlers-Danlos syndrome (EDS), 142–144, *143*
Embolus, 97, 204
Embryo, 118, 131
Emigration, *47,* 48
Emulsifier, 272
Enamel hypoplasia, *324,* 556–557
Enamel pearls, 568–569, *569*
Encephalitis, 277–278
Endocardium, 194
Endocrine imbalances, 97

Endocrine system
  adrenal gland
    acute adrenal insufficiency or adrenal crisis, 173
    adrenocortical insufficiency (*see* Adrenocortical insufficiency)
    hyperadrenalism (*see* Hyperadrenalism)
  disorders, 163
  function of
    adenohypophysis, 161
    endocrine hormones and functions, 161, 162t
    hypophysis, 161
    hypothalamic hormones, 161, 161t
    negative feedback system, 163, *163*
    neurohypophysis, 161
    pituitary hormones, 161, 162t
  hypothalamus and pituitary gland
    diabetes insipidus, 163–164
    growth hormone, hypersecretion of, 164–165
    hypopituitarism, 164
    relationship, *161*
  organs and hormones of, 160–161
    exocrine and endocrine glands, 160, *160*
    hormones, 160
    target cells, 160
  pancreas
    diabetes mellitus, 174, 175t (*see also* Diabetes mellitus)
    fasting plasma glucose test (FPG), 176
    glycated hemoglobin test (A1C), 176
    hormones, 174, 175t
    oral glucose tolerance test (OGTT), 176
  parathyroid gland
    hyperparathyroidism, 170
    hypoparathyroidism, 169–170
  thyroid gland
    follicles, 165
    goiter, 165, *166*
    hyperthyroidism (*see* Hyperthyroidism)
    hypothyroidism (*see* Hypothyroidism)
    triiodothyronine and thyroxine, 165
Endophytic lesions, 12
Environmental agents, 91
Eosinophils, 50, *50*
Ephelides, 615
Ephelis, 422
Epidermis, 103
Epidermolysis acquisita, 323
Epidermolysis bullosa (EB), 323–325, *324*
Epidermolysis bullosa acquisita, 325
EpiPen, 73
Epistaxis, 199
Epithelial rests, 518
Epithelialization, 57
Erosions, 12, *13, 552,* 552–553
Erosive lesions, 332
Erosive oral lichen planus, *369*
Eruption cyst, 528–530
Erythema, 13, *14*
Erythema migrans, 388, *388*
Erythema multiforme (EM)
  drug sensitivity and exposure, 618–619, *619*
  ulcers and inflammatory lesions, 346–347, *347*
Erythematic lesions, 12
Erythematous candida, 372, *372*
Erythroblastosis fetalis, 75, 581
Erythrocytes, 227 (*See also* Red blood cells)
Erythroleukoplakia, 398, *398*
Erythroplakia, 354, 374–375, *375*
Esophageal lichen planus, 368–369
Estimated average glucose (eAG), 176
Euploid cell, 131
Ewing sarcoma, 497
Exacerbation, 34
Excisional biopsy, 94
Exocrine system, 32
Exophthalmos, 168
Exophytic lesions, 12
Exostosis, 486–487, *487*
Expressivity, 128
Exsanguination, 205
Exudate, 48, 48t

F

Facial symmetry, supraorbital aspect, 6, *6*
Factitial injury, 332
Familial colorectal polyposis (*see* Gardner syndrome)
Family violence, 22–5
Fasting plasma glucose test (FPG), 176
Fat tissue neoplasm, 463, *463*
Favre-Racouchot disease, 614, *614*
Fetal alcohol spectrum defects (FASD), 120–122, *121*
Fetus development, 118
Fibrin clot, 248
Fibrinous exudate, 332
Fibrinous lesions, 364
Fibroblasts, 55
Fibromas, *450*, 450–451
Fibromatosis, 459, *459*
Fibroodontoma (*see* Ameloblastic fibroma)
Fibrosarcoma, 459–460
Fibrous dysplasia, 289–291, *290, 291*
Fibrous repair
  angiogenesis, 57
  blood clot formation, 57
  epithelialization, 57
  granulation tissue, 57, *57*
  scar formation, 56–57
  types of, 57
    primary intention, 57, *58*
    secondary intention, 57, *59*
  wound healing
    complications of, *59,* 59–60, *60*
    factors affecting, 57, 59
Field carcinogenesis, 356
Fine-needle aspiration, 94
Fissured lesion, *15,* 16
Fistula, 55, 338
Florid cementoosseous dysplasia, 524, 525
Fluctuant lesion, 15
Fluorosis, 579, *579*
Focal argyrosis, 413, *414*
Focal cementoosseous dysplasia, 524, 525
Focal sclerosing osteomyelitis, *505,* 505–506
Foliate papilla, 454
Follicles, 165
Forchheimer signs, 318
Fordyce granules, *386*, 386–387, *387*
Freckles, 615
Free radical injury, 38–39
Frey syndrome, 464–465
Frictional keratosis, 388–389, *389*

G

Gametes, 125
Gardner syndrome, 510, *510,* 561–562, *562*
Garré osteomyelitis, 488
Gastroesophageal reflux, 552
Gastroesophageal reflux disease (GERD), 273
Gastrointestinal system disorders
  Crohn disease, 274–275
  dysphagia, 272–273
  gastroesophageal reflux disease, 273
  malabsorption syndromes, *276,* 276–277
  peptic ulcer, 273–274
  Peutz-Jeghers syndrome, 275, *275*
Gene, 127
Generalized gingival hyperplasia, 452–453, *453*
Generalized lesion, 10, *10*
Genetic disorders (*see also* Congenital disorders)
  abnormal number of chromosomes, 131, 131
  chromosome structural abnormalities, 131, 131–132
  mosaicism (*see* Mosaicism)
  multifactorial inheritance, 148 (*see also* Cleft lip and/or palate)
  single-gene or mendelian disorders (*see* Single-gene or mendelian disorders)
Genetic material deletion, 131, *131*
Genetic profiling, 97
Genetics
  allele, 127
  chromosomes
    Barr body, 126, *127*
    centromere, 124
    chromatid, 124, *126*
    chromatin, 124
    mitosis and meiosis, 124, *125*
    sex chromosomes, 125
    somatic cells and gametes, 125
    telomeres, 125, *127*
    x chromosome inactivation, 125–127
  and dentistry, 124
  elements
    codominance, 128
    dominant genes, 128
    expressivity, 128
    genotype, 127
    genotype *vs*. phenotypic expression, 129, 130t
    homozygous and heterozygous, 128
    intermediate expression, 128
    penetrance, 128
    phenotype, 128
    recessive and carrier genes, 128
  genes, 127
  genetic disorders
    abnormal number of chromosomes, 131, *131*
    chromosome structural abnormalities, *131,* 131–132
    mosaicism (*see* Mosaicism)
    multifactorial inheritance, 148 (*see also* Cleft lip and/or palate)
    single-gene or mendelian disorders (*see* Single-gene or mendelian disorders)
  locus, 127

Minimum Standard for Genetics Education, 123b
Genokeratoses, 396
Genotype, 127
Geographic tongue (GT), 388, *388*
German measles, 318
Gestational diabetes mellitus (GDM), 176, 186
Ghost teeth, 577, *577*
Giant cell epulis (*see* Peripheral giant cell granuloma (PGCG))
Giant cells, 51, *51*
Gigantism, 89, 164, *164*
Gingiva, 332, *333*
cinnamic aldehyde reaction, *322*
enlargement, *245*
erythematous candida, 372, *372*
fibromatosis, 146–147, 146t
Gingivectomy, 453
Glands of Blandin-Nuhn, 456
Glandular odontogenic cyst, 534
Globodontia, 567–568
Globulomaxillary cyst, *533*, 533–534
Glossitis
anemia, 229, *230*
malabsorption syndrome, 276, *276*
Glycated hemoglobin test (A1C), 176, 176t
Glycosylation, 176
Goiter, 36, *36,* 165, *166*
Gonorrhea, 337–338, *338*
Gorlin cyst (*See* Calcifying odontogenic cyst)
Gorlin sign, 143
Graft *versus* host disease, 619, *619*
Graft-*versus*-host reaction, 77
Granulation tissue, 57, *57*
Granulocytes, 50
Granuloma, 55, *55*
Granulomatous inflammation, 55, *55*
Graves disease, 75, 168
Growth regulators, 86
Gumma, 336

H

Hairy leukoplakia (HL)
HIV infection, 594, *594*
white lesions, *394,* 394–395
Hairy tongue, 391, *391*
Hamartoma, 377, 448, 508
Hand-foot-and-mouth disease, 315–317, *316*
Haploid cells, 125
Haptens, 65
Hard tissue enlargements
exostosis, 486–487
infections, 488
neoplasms
ameloblastoma, 489
calcifying epithelial odontogenic tumor, 489–491
central giant cell granuloma, 492–493
chondrosarcoma, 495–497
Ewing sarcoma, 497
ossifying fibroma, 491–492
osteosarcoma, 493–495
torus palatinus and/or mandibular torus, 485–486
Hashimoto thyroiditis, 166
Health, 3
Health care, 3
Heart defects and dental care, 121b
Heart disorders
congenital heart defects (*see* Congenital heart defects)
dysrhythmias, 210
heart valve defects (*see* Heart valve defects)
Heart murmur, 210
Heart valve defects
common causes of, 213, 213b
congestive heart failure, 216–218, *217*
infective endocarditis, 215–216, *216*
mitral valve prolapse, 214, *214*
rheumatic heart disease, 214–215, *215*
symptoms, 213
treatment, 213–214
Heavy metal pigmentation, 415–416, *416*
Hemangioma, 377, *377, 378*
Hemarthrosis, 249, *250*
Hematocrit, 229
Hematoma, *376*
Hematopoiesis, 227, *228*
Hematopoietic system, 227, *228*
red blood cells (*see* Red blood cells)
white blood cells (*see* White blood cells)
Hematuria, 249
Hemoglobin A1C test, 176
Hemoptysis, 268
Hemostasis
coagulation cascade, 247, *248*
coagulation factors, 247, 247b
fibrin clot, 248
hypercoagulation, 248
platelets, 247, *248*
vascular injury, 247
Hepatocellular carcinoma, 91
Hereditary hypohidrotic ectodermal dysplasia, 558–559, *559*
Herpangina, 317, *317*
Herpes labialis, 310
Herpes simplex virus (HSV) infection
herpetic whitlow, 311, *311*
ocular herpes, 311, *311*
primary herpetic gingivostomatitis, 307–309, *308*, *309*
recurrent herpes simplex infections, 309–311, *310*
types, 307
varicella-zoster virus (*see* Varicella-zoster virus infection)
Herpetic whitlow, 311, *311*
Hiatal hernia, 552
Histamine, 51–52
Histoplasmosis, 597–598
Hodgkin lymphoma, 239–240, *240*
Homeostasis, 3
Homozygous and heterozygous, 128
Hormone therapy, 98
Hormones, 160
Host-*versus*-graft reaction, 77
Human immunodeficiency virus (HIV) infection
human immunodeficiency virus, 591
oral manifestations
candidiasis, *593,* 593–594, *594*
hairy leukoplakia, 594, *594*
human papilloma virus lesions, 595, *595*
neoplastic lesions, 595–596, *596*
oral ulcerations, 596–598, *597*
periodontal diseases, *598,* 598–599
salivary gland disease and xerostomia, 599, *599*
pathogenesis
AIDS-defining conditions, 592b
clinical latency, 591
diagnosis, 591, 592t
seroconversion, 591
viral load, 591
therapy, 593
Humoral immunity, 66–69, *67, 68,* 68b
Hutchinson incisors, 122, *123,* 337, 567, *567*
Hutchinson triad, 337, 567
Hyperacusis, 280
Hyperadrenalism, 94, 173–174
Hypercalcemia, 170
Hypercementosis, 289, 569–570, *571*
Hypercholesterolemia, 195
Hyperchromatic nuclei, 95
Hypercoagulation, 97, 238
Hyperdontia, 559–560, *560*
cleidocranial dysplasia, 560–561, *562*
Gardner syndrome, 561–562, *562*
genetic syndromes, 562
hyperdontia, 559–560, *560, 561*
Hyperglycemia, 174–175
Hyperhidrosis, 144
Hyperinsulinism, 177
Hyperkeratosis, 386
Hyperosmolar hyperglycemic state (HHS), 177, 178t, 184
Hyperplasia, 36, *37*
Hyperplastic candidiasis, 593, *593,* 393–394, *394*
Hyperplastic pulpitis, 553
Hyperreflexia, 169
Hypersensitivity reactions
hygiene hypothesis, 72
peanut butter, 72
red/purple lesions, 370–371, *371*
type I
anaphylactic reactions, 72–73, 73b
atopic reactions, *73,* 73–74
latex hypersensitivity, 74–75, 74b, 75b
localized reactions, 74
type III, 75–76
type IV, *76,* 76–77, *77*
ulcers and inflammatory lesions, 347–349, *348, 349*
Hypertelorism, 140
Hypertension, 199–201, 199t
Hyperthermia, 98
Hyperthyroidism, 75, 94, 168–169, 168t, *169*
Hypertrophy, 35–36, *36*
Hyphae, 373, *373,* 393, *393*
Hypochromic (iron deficiency) anemia, 229–230, *230,* 230t, *231*
Hypodontia, 147
Hypoglycemia, 75, 172, 184
Hypoglycemic unawareness, 177
Hypophosphatasia, 145, 578
Hypophysis, 161
Hypothalamus and pituitary gland disorders
diabetes insipidus, 163–164
growth hormone, hypersecretion of, 164–165
hypopituitarism, 164
relationship, *161*
Hypothyroidism, 166–168, *167*, 167t
Hypoxic cell injury, 39–40, *40*

I

Iatrogenic ulcers, 332, *333*
Idiopathic etiology, 31
Ischemia, 35
Immune complex-mediated reactions, 75–76
Immune deficiency diseases
  primary, 78–79
  secondary, 79
Immune system disorders
  red/purple lesions
    hypersensitivity reactions, 370–371
    lichen planus, 367–370
  soft tissue enlargements (*see* Sjögren syndrome)
  ulcers and ulcer-like lesions
    aphthous ulcers, 341–344
    Behçet syndrome, 344–345
    Crohn disease, 351–352, *352*
    erythema multiforme, 346–347, *347*
    hypersensitivity reactions, 347–349
    lupus erythematosus, 349–351, *351*
    Reiter syndrome, 345–346, *346*
  white lesions, *395,* 395–396
Immune thrombocytopenic purpura, 252, *252*
Immunity
  antigen, 65
  immune response, 65
  major histocompatibility complex, 65
  nonspecific, 65–66
  specific immunity
    active immunity, 70–71
    cell-mediated immunity, *69,* 69–70, *70*
    cellular and chemical components, 66, 67t
    humoral immunity, 66–69, *67, 68,* 68b
    organs associated with, 66
    passive immunity, 71
Immunoglobulins (Ig), 68
Immunopathology
  autoimmune disease, 77–78, *78,* 78t
  hypersensitivity reactions (*see* Hypersensitivity reactions)
  immune deficiency diseases
    primary, 78–79
    secondary, 79
Immunotherapy, 98
Impetigo, 619, *620*
Incisional biopsy, 94
Incisive canal cyst (*see* Nasopalatine canal cyst)
Incontinentia pigmenti, 559
Increased vascular permeability, *47,* 48
Incubation period, 34
Infarction, 198
Infective endocarditis, 215–216, *216*
Inflammatory lesions (*see* Traumatic lesions)
Inflammatory cysts, 518
Inflammatory process
  cellular components, *50*
    agranulocytes, 50–51, *51,* 51b
    granulocytes, 50
    mast cell, 51
  chemical mediators
    endogenous, 51–52
    exogenous, 51
Influenza, 264–265
Innate immunity, 65–66
Integumentary system, 32
Intentional tattooing, 415, *415*
Interleukin-1 (IL-1), 52
Intermediate gene expression, 128
Intracellular calcium imbalance, *40*
Intramucosal nevus, *422*
Intrinsic factor (IF), 233
Inversions, 131, *131*
Involution, 377
Involution failure, 118
Ionizing radiation, 98
Iron deficiency anemia, 229–231, *231*, 230t
Irreversible cellular injury
  apoptosis, 40, *40*
  necrosis
    caseous necrosis, 40–41, *41*
    coagulative, 41, *41*
    liquefactive, 41, *41*
Irreversible pulpitis, 553
Irritant contact dermatitis (ICD), 77, *77*
Ischemia, 204

J

Jaundice, 229, *229*
Junctional nevus, 420

K

Kaposi sarcoma, 105, 364, 595–596, *596*
Karyotype, 127, *129*
Keloids, 59, *59,* 615, *615*
Keratinization, 437
Keratinocytes, 102, 435
Keratoacanthoma, 101, 440–441, *441*
Keratoconjunctivitis sicca, 457
Kinin system, 52
Klinefelter syndrome, 134–135
Koebner phenomenon, 395
Koplik spots, 317, *318*

L

Labial varices, 14, *14*
Labile cells, 86
Laminar blood flow, 194
Langerhans cells, 69, *69*
Langerhans cell disease, 539–540, *540*
Latent period, 34
Lateral periodontal cyst, 527–529
Latex hypersensitivity, 74–75, 74b, 75b
Laugier-Hunziker syndrome (LHS), 423–424, *424*
Lead-line stain, 415, *416*
Leiomyoma, 461, *461*
Leishmaniasis, 622–623, *623*
Lentigo maligna, 423
Lentigo maligna melanoma, 104, *104*
Leukemia, 243–245, 244t, *245*
Leukocyte emigration/transmigration, *47,* 48, *49*
Leukocytosis, 53
Leukoedema, 387, *387*
Leukopenia, 99
Leukoplakia, 88, *88,* 386, *397*, 397–400, *399, 400*
Leukotrienes, 52
Libman-Sacks endocarditis, 350
Lichen planus (LP), 619–620, *620*
  red/purple lesions, 367–370, *368*
  white lesions, *395,* 395–396
Lichenoid reactions, 367, 368
Linea alba, 389, *389*
Linear gingival erythema, 598, *598,* 598–*598*
Lingual varicosity, *376*
Lip lesions, Crohn disease, 352, *352*
Lipoma, 463, *463*
Liquefactive necrosis, 41, *41*
Lisch nodules, 469, *469*
Lobodontia, 567
Localized lesion, 10, *10*
Locus, 127
Lower respiratory diseases
  pneumonia, 265–267
  tuberculosis, 267b, 267–268, *268*, 269b
Ludwig angina, 55, *56*
Lumen, 518
Lung cancer, 108–109
Lupus erythematosus
  scalp and cutaneous lesions, 620, *621*
  ulcers and inflammatory lesions, 349–351, *350, 351*
Lupus malar rash, 350, *350*
Lymphadenopathy, 6–7, *8*
Lymphangioma, *378,* 378, *471*, 471–472, *472*
Lymphocytes, *50,* 51, 54
Lymphoid hyperplasia, *453,* 453–454, *454*
Lymphoma
  Hodgkin lymphoma, 239–240, *240*
  leukemia, 243–245, 244t
  multiple myeloma, 245–247, *246*
  non-Hodgkin lymphoma, 240–243, *241–243*
Lysosomal enzymes, 54
Lysosomes, 54

M

Macrodontia, 563, *564*
Macroglossia, 164, *165*
Macrophages
  chronic inflammation, 53–54
  functions, 50–51, 51b
  immune response, *69,* 69–70, *70*
Macrovascular disease, 175
Macule, 11, *11,* 422, *423*
Maculopapular rash, 71
Major aphthous ulcer, 597, *597*
Major histocompatibility complexes (MHC), 65
Malabsorption syndromes, 275–277, *276*
Malignant neoplasms
  vs. benign neoplasms, 88t, 89
  carcinogenesis, 90–91
  carcinoma, 89
  clinical characteristics, 88t
  histology, 89, *89*
  local growth and distant metastasis, 91–93, *92, 93*
  nomenclature, 89–90, 90t
  sarcoma, 89
Malignant skin lesions
  basal cell carcinoma, 610, 611, *611*
  melanoma, 611–612, *612*
  squamous cell carcinoma, 610, 611, *611*
Mandibulofacial dysostosis, 142, *142*
Manifestation, 34
Marble bone disease, 511
Marfan syndrome, *139,* 139–140
Margination, *47,* 48
Mast cell, *50,* 51

Measles (*see* Rubeola)
Median palatine cyst, 535
Median rhomboid glossitis, 373, *373*
Megaloblastic anemia, 233–234, *234*
Melanin, 410
Melanocytes, 410
Melanoma, 14, 102–107, *103*–105, 105b–106b (*see also* Oral melanoma)
Melanosomes, 410
Membrane attack complex (MAC), 52
Memory cells, 67–68
Mendelian disorders (*see* Single-gene disorders)
Meningitis, 277–278
Metaplasia, 36–37, *37*
Metastatic breast cancer, 91, *93*
Metastatic calcifications, 512
Metastatic malignant melanoma, 103, *104*
Metronidazole, 599
Microangiopathy, 174, 178, 180, *180*
Microdontia, 562–563, *563*
Microinvasive squamous cell carcinoma (SCC), 92, *93*
Migraine headache, 281–282
Mild epithelial dysplasia, 399, *399*
Milia, 615, *616*
Minocycline tissue staining, 416–417, *417*
Minor aphthous ulcer, 597, *597*
Mitosis and meiosis, 124, *125*
Mitotic figures, 95, *95*
Mitral valve prolapse (MVP), 214, *214*
Mitten-like scarring, *324*
Mixed lesion, 16, *17*
Moderate epithelial dysplasia, 399, *399*
Molecular profiling, 97
Moles, 615
Moniliasis (*see* Acute pseudomembranous candidiasis)
Monocyte, 50, *50*
Monosomy, 131
Monosomy X (*see* Turner syndrome)
Morbidity, 32, 34
Morsicatio buccarum, 334
Mortality, 34
Mosaicism
  Klinefelter syndrome (testicular dysgenesis), 134–135
  trisomy 21 (Down syndrome), 132–134
  Turner syndrome (monosomy X), 135–136
Motile phagocytes, 50
Mucocele, 305–307, *306*
Mucoepidermoid carcinoma, 465–466, *466*
Mucosal nevus, 420
Mucositis, 98–99, *99*
Mucous membrane pemphigoid (MMP), 320–322, *321*
Mucous patches, 336, *336*
Mucus extravasation phenomenon, 305
Mulberry molars, 122, *123,* 336–337, 567, *567*
Multifactorial inheritance, 148
Multilocular radiopaque, 17, *17*
Multiple endocrine neoplasia syndrome, type 2B (MEN 2B), 470–471, *471*
Multiple hamartoma syndrome, 451
Multiple lesions, 10, *11*
Multiple myeloma, 245–247, *246*
Mumps, *456*, 456–457
Mycobacteria, 454
Myxedema, 167

N

Nasopalatine canal cyst, 534–535, *535*, *536*
Nasopalatine duct cyst (*see* Nasopalatine canal cyst)
Natural immunity, 65–66
Natural killer (NK) cells, 69
Natural rubber latex (NRL) proteins, 74
Necrosis
  caseous necrosis, 40–41, *41*
  coagulative, 41, *41*
  liquefactive, 41, *41*
Necrotizing sialometaplasia, 334–335
Necrotizing ulcerative gingivitis (NUG), 339–340, 598, *598*
Needle biopsy, 94
Neoplasm, 37–38 (*see also* Salivary gland neoplasms)
  benign neoplasms
    brain tumor, 89
    clinical characteristics, 87, 88t
    endocrine gland tumors, 89
    histology, 89, *89*
    vs. malignant neoplasms, 88t
    nomenclature, 90t
  cementoblastoma, 506–508, *507*
  diagnosis
    biomarkers, 94
    brush biopsy, 94, *94*
    cancer screening methods, 94
    cell differentiation level, 95
    cell size and shape, 95
    clinical symptoms, 94
    microscopic examination, 94
    mitotic figures, 95, *95*
    oropharyngeal cancer development sites, 94b
    tumor grading and staging, 95, 96b, 96t
  Gardner syndrome, 510, *510*
  hard tissue enlargements
    ameloblastoma, 489
    calcifying epithelial odontogenic tumor, 489–491
    central giant cell granuloma, 492–493
    chondrosarcoma, 495–497
    Ewing sarcoma, 497
    ossifying fibroma, 491–492
    osteosarcoma, 493–495
  vs. hyperplasia, 88, *88*
  malignant neoplasms
    vs. benign neoplasms, 88t, 89
    carcinogenesis, 90–91
    carcinoma, 89
    clinical characteristics, 88t
    histology, 89, *89*
    local growth and distant metastasis, 91–93, *92, 93*
    nomenclature, 89–90, 90t
    sarcoma, 89
  odontoma, 508–509, *509*
  osteoma, 508–510, *510*
  paraneoplastic syndromes, 95–97
  pigmented lesions (*see* Oral melanoma)
  prevention strategies, 99, 100b
  radiolucent lesions
    adenomatoid odontogenic tumor, 536–538
    ameloblastic fibroma (fibro-odontoma), 538–539
    langerhans cell disease, 539–541
    odontogenic myxoma, 538
  radiopaque lesions
    cementoblastoma, 508
    Gardner syndrome, 510
    odontoma, 508
    osteoma, 508–509
  red/purple lesions
    erythroplakia, 374–375, *375*
    Kaposi sarcoma, 374, *374*
  soft tissue enlargements
    fat tissue neoplasm, 463, *463*
    fibromatosis, 459, *459*
    fibrosarcoma, 459–460
    leiomyoma, 461, *461*
    neurilemoma, 460, *460*
    neurofibroma, 460–461, *461*
    rhabdomyoma, 462, *462*
    salivary gland (*see* Salivary gland neoplasms)
  therapy
    antiangiogenesis therapy, 98
    chemotherapy, 98
    complementary therapies, 98, 98b
    hormone therapy, 98
    hyperthermia, 98
    immunotherapy, 98
    photodynamic therapy, 98
    radiation therapy, 98
    side effects of, 98–99, *99*
    surgical procedures, 97–98
    treatment choice, 97
Nephropathy, 178
Nervous system disorders
  Bell palsy, 279–280, 279b, *280*
  burning mouth syndrome, 282, 282b
  meningitis and encephalitis, 277–278
  migraine headache, 281–282
  Parkinson disease, *278*, 278–279
  trigeminal neuralgia, 280–281
Neurilemoma, 460, *460*
Neurofibroma, 460–461, *461*
Neurofibromatosis, type 2B, 468–470, *469*
Neurohypophysis, 161
Neuropathy, 175
Neutropenia, 238–239, *239*
Nevi, 615–616, *616*
Nevoid basal cell carcinoma syndrome, 530
Nevus (blue nevus), *14*, 15, 420–422, *422*
Nicotine stomatitis, *390*, 390–391
Nikolsky sign, 319
Nocturia, 218
Nodule, 12, *12*
Nondisjunction, 131
Non-Hodgkin lymphoma, 240–242, *241, 242*, 596, *596*
Nonspecific immunity, 65–66
Nonthrombocytopenic purpura, 252
Nonvital tooth, 520
Normal cartilage, *89*
Normal cell growth, 86
Nosocomial pneumonia, 265

O

Obstructive pulmonary diseases
  asthma, 269–270, 269b
  chronic obstructive pulmonary disease, 270–271
  cystic fibrosis, *271*, 271–272
Ocular herpes, 311, *311*
Odontogenic cysts, 518
Odontogenic keratocyst, 530–531
Odontogenic myxoma, 538
Odontoma, 508–509, *509*
Oligogenic inheritance, 138
Oncogenes, 90
Oophoritis, 456
Opportunistic infections, 79
Opsonization, *47,* 48
Oral and perioral scarring, epidermolysis bullosa, *324*
Oral cancers, 100, 100t
Oral glucose tolerance test (OGTT), 176
Oral melanoma, 424–426, *425*
Oral melanotic macule, 422–423, *423*
Oral metastatic cancer, 110
Oral squamous papilloma, 435–436, *436*, *437*
Oral submucous fibrosis (OSF), 400–401, *401,* 420
Oral tuberculosis ulcer, 268, *268*
Orchitis, 456
Orthopnea, 217
Ossifying fibroma, 491–492, *492*
Osteoarthritis, 283, *283*
Osteogenic sarcoma (*see* Osteosarcoma)
Osteoma, 509–510, *510*
Osteomyelitis, 525–526, *527*
Osteopenia, 181
Osteopetrosis, 511–512
Osteoporosis, 181, 285–286, 285b, *286*
Osteosarcoma, 493–495, *494*

P

Paget disease, *288,* 286–289, *289*
Painful oral ulcerations, 98–99, *99*
Palatal nevus, *422*
Palpation, 449
Pancreatic disorders
  diabetes mellitus, 174, 175t (*see also* Diabetes mellitus)
  fasting plasma glucose test (FPG), 176
  glycated hemoglobin test (A1C), 176
  hormones, 174, 175t
Papillary cystadenoma lymphomatosum, 465, *465*
Papillary hyperplasia, 439–440, *439*
Papillary lesion, 15, *15*
Papillon-Lefèvre syndrome (PLS), 144, 144–145
Papule, 12, *12*
Paradental cyst, 528
Parafollicular cells, 165
Parafunctional dental habits, 551
Parafunctional jaw movements, 278
Paramyxoviridae virus infections (*see* Rubeola)
Paraneoplastic syndromes, 95–97
Parathyroid gland disorders
  hyperparathyroidism, 170
  hypoparathyroidism, 169–170
Parkinson disease, *278*, 278–279
Paroxysmal nocturnal dyspnea, 217
Paroxysms, 269
Partial denture stomatitis, 373, *373*
Parulis, 395
Passive immunity, 71
Patch, 11
Patent ductus arteriosus (PDA), 210, *210*
Paterson-Brown Kelly syndrome, 231
Pathologic murmurs, 213
Pathology
  definition, 3
  disease manifestations
    cellular adaptation (*see* Adaptive cellular changes)
    irreversible cellular injury, *40,* 40–41, *41*
    reversible cellular injury, 38–40, *40*
  etiology, 30–31
  pathogenesis, 34
  resistance and susceptibility
    age, 32
    environmental exposure, 32–33
    first-line defense systems, 32
    genetic influences, 31
    immune system, 31–32
    lifestyle choices, 32
    modifiable *vs.* nonmodifiable risk factors, 33
    multiple risk factors, 33
    preexisting conditions, 33
    risk factors, 31b
    stress, 32, 32b
Pavementing, *47,* 48
Pedunculated lesion, 12, *13*
Pemphigoid
  bullous pemphigoid, 322, *322*
  mucous membrane pemphigoid, 320–322, *321*
Pemphigus vulgaris, 318–320, *319*
Penetrance, 128
Peptic ulcer, 273–274
Percussion, 553
Periapical cementoosseous dysplasia, 524
Periapical cyst (*see* Radicular cyst)
Periapical granuloma, 519–521
Periodontal diseases
  acute necrotizing periodontitis, *598,* 598–599
  linear gingival erythema, 598, *598*
  necrotizing ulcerative gingivitis, 598, *598*
  pain control and management, 599
Periodontal ligament space widening, 19, *19*
Periodontitis, 145
Peripheral artery disease (PAD), 203
Peripheral giant cell granuloma (PGCG), 364–365, *365*
Peripheral neuropathy, 178
Peripheral ossifying fibroma, *451*, 451–452, *451, 452*
Peristalsis, 272
Peritoneal cavity, 91
Perlèche, 373, 616, *616* (*see also* Angular cheilitis)
Permanent cells, 86
Pernicious anemia, 233
Persistent generalized lymphadenopathy (PGL), 591
Pertussis, 266
Petechiae, 365–367, *366*
Peutz-Jeghers syndrome, 109, 275, *275*
Phagocytes, 52
Phagocytosis, *47,* 48, *49*
Phagosome, 54–55
Philadelphia chromosome, 90
Phlebolith, 377, 513
Phlebotomy, 238
Photodynamic therapy, 98
Photophobia, 147, 458
Physiologic murmurs, 213
Physiologic pigmentation, 12, *13,* 410–412, *411*
Pigmented lesions
  associated with drugs
    azidothymidine, 417, *417*
    betel quid use, 418, 419b, 420, 420b, *421*
    minocycline tissue staining, 416–417, *417*
    smoking-associated melanosis, 417–418, *418*
  congenital or genetic disorders
    nevus, 420–422, *422*
    oral melanotic macule, 422–423, *423*
  disease-associated melanosis (*see* Laugier-Hunziker syndrome (LHS))
  metal pigmentations
    heavy metal pigmentation, 415–416, *416*
    intentional tattooing, 415, *415*
    metal accumulation, 413–414
    titanium implants, 414–415, *415*
  neoplasms (*see* Oral melanoma)
  normal pigment variations
    physiologic pigmentation, 410–412
  traumatic or inflammatory lesions
    amalgam tattoo, 413, *414*
    chronic inflammation, 412
    ethnic tattoo, *412,* 412–413
    metallic particles, 412
    smoker's melanosis, 412
Pink tooth of Mummery, 555
Pityriasis, 616, *616*
Plaque, 12, *13*
Plasma cell gingivitis, 370
Plasma cells, 54, 66–67
Plasma-derived chemical mediators, 52
Platelet plug, 247, *248*
Platelet-activating factor, 52
Pleomorphic adenoma
  carcinoma ex-mixed tumor, 464
  dental implications, 464
  differential diagnosis, 464
  epidemiology, 463
  etiology, 463
  Frey syndrome, 464–465
  microscopic and radiographic features, 464, *464*
  pathogenesis, 463
  perioral and intraoral characteristics, *463,* 463–464, *464*
  treatment and prognosis, 464, *464*
Pleomorphism, 95
Pleural cavity, 91
Plumbism, 415
Plummer-Vinson syndrome, 230, 231
Pluripotential stem cells, 228
Pneumonia, 265–267
Poison oak, 616, *617*
Polycythemia, 211, 237–238, *238*

Polydipsia, 163
Polymorphonuclear neutrophil, 50, *50*
Polymorphous low-grade adenocarcinoma, *467,* 467–468
Polyphagia, 176
Polyposis, 510
Polyps, 109
Polyuria, 163
Poorly defined margin, 10, *11,* 17–18, *18*
Porphyria, *581,* 581–582
Postherpetic neuralgia (PHN), 314
Prayer sign, 181
Precystic epithelial proliferation, 519
Prediabetes, 176
Preformed chemical mediator, 51–52
Prehypertension, 200
Premalignant skin lesions
  actinic cheilitis, 613, *614*
  actinic keratosis, 613, *613*
Primary herpetic gingivostomatitis, 307–309, *308, 309*
Primary immune response, 67
Primary tumor, 93
Primordial cyst, 531
Prognosis, 34
Proliferative verrucous leukoplakia, 398, *398*
Proprioceptive ability loss, 233
Prostaglandins, 52
Prostate cancer, 108
Prostate-specific antigen (PSA), 94
Proto-oncogenes, 86, 90
Pruritic lesions, 395
Pseudoanodontia, 167
Pseudocysts, 518
Pseudomembrane, 16, *16*
Pseudomembranous candidiasis, 593, *593*
Pseudomembranous plaques, 393
Psoriasis, 102
Psychogenic illness, 31
Pterygium, 6, *6*
Pulmonary hypertension, 210
Pulp stones
  cellular alteration, 554
  dental radiographs, 553–554, *554*
  etiology, 554
  external resorption, 555–556, *556*
  formation of, 554
  internal resorption, 555, *555*
Pulpitis, 553
Purpura, 365–367, *366*
Purulent exudate, 12
Pustule, 12
Pyogenic granulomas, 363–364, *364*
Pyostomatitis vegetans, 351–352, *352*

Q

Quid, 418, *421*
Quiescent cells, 86

R

Radiation caries, 99, *99*
Radiation therapy, 98
Radicular bone, 553
Radicular cyst, 518, *521,* 521–522
Radiolucent lesions, 16, *17*
  developmental cysts
    calcifying odontogenic cyst (Gorlin cyst), 531–533
    dentigerous cyst, 528
    eruption cyst, 528–530
    glandular odontogenic cyst, 534
    globulomaxillary cyst, 533–534
    lateral periodontal cyst (botryoid odontogenic cyst), 527–528
    nasopalatine canal cyst (incisive canal cyst, nasopalatine duct cyst), 534–536
    odontogenic keratocyst, 530–531
    static bone cyst (Stafne bone defect, static defect), 536
  infections, 525–526
  neoplasms
    adenomatoid odontogenic tumor, 536–538
    ameloblastic fibroma (fibro-odontoma), 538–539
    Langerhans cell disease, 539–541
    odontogenic myxoma, 538
  traumatic/inflammatory lesions
    aneurysmal bone cyst, 522–523
    cementoosseous dysplasia, 523–525
    periapical granuloma, 519–521
    radicular cyst, 521–522
    traumatic bone cyst, 523
Radiopaque lesions, 16, *17*
  calcified lymph nodes, 512, *512*
  congenital/genetic disorders, 511–512
  neoplasms
    cementoblastoma, 508
    Gardner syndrome, 510
    odontoma, 508
    osteoma, 508–509
  traumatic/inflammatory lesions
    focal sclerosing osteomyelitis, 505–506
    osteomyelitis with diffuse lesions, 506
Ramsay Hunt syndrome, 314
Ranula, 305, *455,* 455–456
Raynaud disease, 205, *205*
Raynaud phenomenon, 620–621
Recessive genes, 128
Recurrent aphthae, 309
Recurrent aphthous ulcers (RAU), 342–344, *342–343*
Recurrent herpes simplex infections, 309–311, *310*
Recurrent herpes zoster, 309
Recurrent herpetic stomatitis, 597, *597*
Red blood cells
  development stages, 228, *228*
  diseases
    anemia (*see* Anemia)
    polycythemia, 237–238, *238*
  life span, 228
Red/purple lesions
  immune system disorders
    hypersensitivity reactions, 370–371
    lichen planus, 367–370
  infections (*see* Candidiasis)
  neoplasms
    erythroplakia, 374–375, *375*
    Kaposi sarcoma, 374, *374*
  traumatic/inflammatory lesions
    peripheral giant cell granuloma, 364–365, *365*
    petechiae, ecchymoses, and purpura, 365–367
    pyogenic granulomas, 363–364, *364*
  vascular malformations
    congenital hemangioma, 377, *377*
    hereditary hemorrhagic telangiectasia, 378–379, *379*
    lymphangioma, *378,* 378
    varicosity, 375–377
Reed-Sternberg cell, 240, *240*
Regional odontodysplasia, 577, *577*
Regurgitation, 213
Reiter syndrome, 345–346, *346*
Relapse, 34
Residual cyst, 522
Resolution, 34
Respiratory system disorders
  lower respiratory tract (*see* Lower respiratory diseases)
  obstructive pulmonary diseases (*see* Obstructive pulmonary diseases)
  upper respiratory tract (*see* Upper respiratory diseases)
Retinopathy, 178
Reverse smoking, 390
Reversible cellular injury
  free radical injury, 38–39
  hypoxic cell injury, 39–40, *40*
  intracellular calcium imbalance, *40*
Reversible pulpitis, 553
Reye syndrome, 265
Rheumatic heart disease, 214–215, *215*
Rhinophyma, 617, *617*
Root resorption, 18, *18*
Rootless teeth, 575–577
Rosacea, 617, *617*
Rough/papillary surface lesions
  infections
    human papillomavirus risk types, 434–435, 434t
    oral squamous papilloma, 435–436, *436, 437*
  papillary hyperplasia (*see* Papillary hyperplasia)
  premalignant/malignant lesions
    keratoacanthoma, *440,* 440–441, *441*
    verrucous carcinomas, *441,* 441–442, *442*
Rubella, 318
Rubeola, 317–318, *318*

S

Salivary gland disease, 599, *599*
Salivary gland neoplasms
  acinic cell carcinoma, 466–467, *467*
  minor salivary gland malignancies
    adenoid cystic carcinoma, 468, *468*
    polymorphous low-grade adenocarcinoma, *467,* 467–468
  mucoepidermoid carcinoma, 465–466, *466*
  papillary cystadenoma lymphomatosum, 465, *465*
  pleomorphic adenoma, *463,* 463–465, *464*
Sarcoidosis, 454–455, *455,* 620, *621*
Sarcoma, 89, 353
Schwannoma, 460, *460*
Sclerodactyly, 621, *621*
Scleroderma, 620–622
Sclerotic bone, 505
Seborrheic keratosis, 101, 618, *618*
Secondary immune response, 67

Secondary immunodeficiency disease, 79
Seeding, body cavity, 93, *93*
Selective immunoglobulin A deficiency (SIgAD), 78–79
Self-tolerant cell, 66
Septicemia, 55
Sequela of disease, 34
Sequestrum, 526
Seroconversion, 591
Serotonin, 52
Serous exudate, 48
Severe epithelial dysplasia, 399, *399*
Sex chromosomes, 125
Sex-linked dominant disorder, 137
Shingles, 314–315, *315*
Shovel-shaped incisors, 564, *564*
Shunt, 209
Sickle cell disease (SCD), 235–236, *236*, 236t
Sign, 34
Single lesion, 10, *10*
Single-gene disorders
  autosomal dominant, 136, *136,* 138b
  autosomal recessive, *136,* 137, 138b
  cleidocranial dysplasia, 140–142
  ectodermal dysplasia, 147–148
  Ehlers-Danlos syndrome, 142–144
  gingival fibromatosis, 146–147
  Marfan syndrome, 139–140
  multifactorial inheritance, 148
  oligogenic inheritance, 138
  Papillon-Lefèvre syndrome, 144–145
  sex-linked dominant, 137
  Treacher Collins syndrome, 142
  X-linked recessive, *136,* 137, 138b
Sjögren syndrome, 457–458, *458*
Skeletal system disorders, 282
  fibrous dysplasia, 289–291, *290, 291*
  osteoarthritis, 283, *283*
  osteoporosis, 285–286, 285b, *286*
  Paget disease, *288,* 286–289, *289*
  rheumatoid arthritis, 283–285
  temporomandibular disorders, 291–293, 291b, 292b
Skin lesions
  benign
    acrochordon, 613–614, *614*
    comedones, 614, *614*
    eczema, 614–615, *615*
    ephelides, 615
    keloids, 615, *615*
    milia, 615, *616*
    nevi, 615–616, *616*
    perlèche, 616, *616*
    pityriasis, 616, *616*
    poison oak, 616, *617*
    psoriasis, 617, *617*
    rhinophyma, 617, *617*
    rosacea, 617, *617*
    seborrheic keratoses, 618, *618*
    solar lentigo spots, 615, *615*
    urticaria, 618, *618*
    xanthelasma, 618, *618*
  Burn Index, 610
  diseases
    erythema multiforme, 618–619, *619*
    graft *versus* host disease, 619, *619*
    impetigo, 619, *620*
    leishmaniasis, 622–623, *623*
    lichen planus, 619–620, *620*
    lupus erythematosus, 620, *621*
    sarcoidosis, 620, *621*
    scleroderma, 620–622
    vitiligo, 622, *622*
    warts, 622
  malignant
    basal cell carcinoma, 610, 611, *611*
    melanoma, 611–612, *612*
    squamous cell carcinoma, 610, 611, *611*
  premalignant
    actinic cheilitis, 613, *614*
    actinic keratosis, 613, *613*
  skin discolorations, 609
  sun exposure, 609, *609*
Smoker's melanosis, 412
Smoking-associated melanosis, 417–418, *418*
Smooth surface texture, 15, *15*
Snuff dippers keratosis, 397, *397*
Soft tissue enlargements
  developmental cysts
    cervical lymphoepithelial cyst, 472–473, *473*
    dermoid cysts, 474, *474*
    thyroglossal tract cyst, *473,* 473–474
  genetic and congenital disorders
    lymphangioma, *471,* 471–472, *472*
    multiple endocrine neoplasia syndrome, type 2B, 470–471, *471*
    neurofibromatosis, type 2B, *469,* 469–470
  immune system disorders (*see* Sjögren syndrome)
  infections
    bacterial sialadenitis, 457
    mumps, *456,* 456–457
  neoplasms
    fat tissue neoplasm, 463, *463*
    fibromatosis, 459, *459*
    fibrosarcoma, 459–460
    leiomyoma, 461, *461*
    neurilemoma, 460, *460*
    neurofibroma, 460–461, *461*
    rhabdomyoma, 462, *462*
    salivary gland (*see* Salivary gland neoplasms)
  traumatic/inflammatory lesions
    causes, 448
    fibromas, *450,* 450–451
    generalized gingival hyperplasia, 452–453, *453*
    lymphoid hyperplasia, *453,* 453–454, *454*
    peripheral ossifying fibroma, *451,* 451–452, *452*
    ranula, *455,* 455–456
    sarcoidosis, 454–455, *455*
    traumatic neuromas, 449–450
Solar cheilosis, 613, *614*
Solar keratosis (*see* Actinic keratosis)
Solar lentigines, 423
Solar lentigo spots, 105–106, 615, *615*
Somatic cells, 125
Speckled erythroleukoplakia, 354
Speckled leukoplakia, 374, 398, *398*
Spongiosis, 371
Squamous cell carcinoma (SCC), 101–102, *102*, 353–356, *354, 355,* 610
Squamous cell carcinoma (SCC) in situ, 91, *93*
Stable cells, 86
Static bone cyst, 536
Stellate reticulum, 568
Stevens-Johnson syndrome, 346, *347*
Stress, 32, 32b
Stroke, *206*, 206–208
Superficially invasive squamous cell carcinoma, 399, *400*
Supernumerary teeth development, 560, *561*
Supraorbital aspect, facial symmetry, 6, *6*
Symblepharon, 321, *321*
Symptom, 34
Synthesized chemical mediators, 52
Syphilis, 335–337, *336*, 336b
Systemic lupus erythematosus, *78* (*see also* Lupus erythematosus)

T

T cytotoxic cell, 69
T helper cell, 66
T lymphocytes, 69
Talon cusp, 564–565, *565*
Target cells, 69, 160
Tattoo, 106
Tattooing, *412,* 412–413
Taurodontism, 569, *570*
Tay-Sachs disease, 38, *39*
Teeth abnormalities
  developmental abnormalities
    color alterations (*see* Teeth color alterations)
    decreased number of teeth (*see* Anodontia)
    increased number of teeth (*see* Hyperdontia)
    macrodontia, 563, *564*
    microdontia, 562–563, *563*
    shape alterations (*see* Teeth shape alterations)
    structural alterations (*see* Teeth structure alterations)
  inflammation
    enamel hypoplasia, 556–557
    pulp stones, 553–556
    pulpitis, 553
  postdevelopmental abnormalities
    abrasion, 551–552, *552*
    attrition, 550–551, *551*
    erosion, *552,* 552–553
Teeth color alterations
  fluorosis, 579, *579*
  hemolytic anemia
    clinical manifestation, 581
    erythroblastosis fetalis, 581
    RBC breakdown products, 580–581
    treatment, 581
  pigment incorporations, 578–579
  porphyria, *581,* 581–582
  tetracycline staining, 579–580, *580*
Teeth shape alterations
  crowns of teeth
    accessory cusps, 564–565
    congenital syphilis, 566–567, *567*
    fusion, 566, *566*
    gemination, 566–567, *567*
    globodontia, 567–568

lobodontia, 567
shovel-shaped incisors, 564, *564*
teeth roots
accessory roots, 568, *568*
concrescence, 569, *571*
dilaceration, 568, *568*
enamel pearls, 568–569, *569*
hypercementosis, 569–570, *571*
taurodontism, 569, *570*
Teeth structure alterations
amelogenesis imperfecta
enamel development stages, 572
enamel structure loss, 573
hypocalcified forms, 572
hypomaturation type, 572
radiographic pattern, 573
treatment, 573
calcified components, 570–571
dens invaginatus
coronal dens invaginatus, 573–574
enamel surface, 573
radicular dens invaginatus, 574
dentinal dysplasia
coronal, 576–577
radicular, 575–576
dentinogenesis imperfecta
clinical appearance, 575, *575*
clinical finding, 574
radiographic appearance, 575, *575*
secondary dentin formation, 575
treatment, 575
enamel hypoplasia
environmental factors, 572–573
malnutrition, 571
systemic illness, 571
treatment, 573
hypophosphatasia, 578
regional odontodysplasia, 577, *577*
vitamin D-resistant rickets, 578, *578*
Telangiectasia, 378–379, *379,* 617
Telomeres, 125, *127*
Temporomandibular disorders (TMDs), 291–293, 291b, 292b
Tensile strength, 551
Teratogenic agents, 118, 119t, *120*
Teratoid cyst, 474
Teratology, 118
Termination, *47,* 48
Testicular dysgenesis (*see* Klinefelter syndrome)
Tetany, 169
Tetracycline staining, 579–580, *580*
Tetralogy of Fallot (TOF), *210,* 210–211
Thalassemia, *231*, 231–233, *232*
Thrombi, 97
Thrombocytopenia, 99, 251–252, *252*
Thrombocytosis, 97
Thromboembolic venous disorders, 205–206, 206b
Thrombus, 194, 377
Thrush (*see* Acute pseudomembranous candidiasis)
Thyroglossal tract cyst, *473,* 473–474
Thyroid gland disorders
follicles, 165
goiter, 165, *166*
hyperthyroidism, 168–169, 168t, *169*
hypothyroidism, 166–168, *167*, 167t
triiodothyronine and thyroxine, 165
Thyroid storm, 168
Tissue sloughing, 348, *349*
Titanium implants, 414–415, *415*
Tobacco
leukoplakia, 88, *88*
verrucous carcinoma, 88, *88*
Togavirus infections, 318
Tonsilloliths, 513
Toothpaste allergy-cinnamic aldehyde, 348, *348*
TORCH syndrome, 122–123, *123*
Torus palatinus/mandibular torus, 485–487, *487*
Trait, 125
Transient ischemic attack (TIA), 207
Translocation, 90, 131, *131*
Transmigration, *47,* 48
Transposition of the great arteries (TGA), 211, *211*
Traumatic bone cyst, 523, *523*
Traumatic neuromas, 449–450
Traumatic lesions
pigmented lesions
amalgam tattoo, 413, *414*
chronic inflammation, 412
ethnic tattoo, *412,* 412–413
metallic particles, 412
smoker's melanosis, 412
radiolucent lesions
aneurysmal bone cyst, 522–523
cementoosseous dysplasia, 523–525
periapical granuloma, 519–521
radicular cyst, 521–522
traumatic bone cyst, 523
radiopaque lesions
focal sclerosing osteomyelitis, 505–506
osteomyelitis with diffuse lesions, 506
soft tissue enlargements
causes, 448
fibromas, *450,* 450–451
generalized gingival hyperplasia, 452–453, *453*
lymphoid hyperplasia, *453,* 453–454, *454*
peripheral ossifying fibroma, *451,* 451–452, *452*
ranula, *455,* 455–456
sarcoidosis, 454–455, *455*
traumatic neuromas, 449–450
ulcers and ulcer-like lesions
necrotizing sialometaplasia (*see* Necrotizing sialometaplasia)
traumatic ulcers (*see* Traumatic ulcers)
vesicular lesions (*see* Mucocele)
white lesions
cheek chewing, *389,* 389–390
chemical and thermal burns, 391–392, *392*
frictional keratosis, 388–389, *389*
geographic tongue, 388, *388*
hairy tongue, 391, *391*
linea alba, 389, *389*
Traumatic ulcers, 332–334, *333, 334*
Treacher Collins syndrome (TCS), 142, *142*
Trigeminal neuralgia, 280–281
Trismus, 457
Trisomy 21, 131–134, *131*
Tuberculosis, 267–269, 267b, *268*, 269b
Tumor, 12
Tumor necrosis factor (TNF), 52
Tumor staging, 95
Tumor-suppressor genes, 86, 90
Turner syndrome, *135,* 135–136
Type 1 diabetes, 176–183
Type 2 diabetes, 183–185
Type I hypersensitivity reactions
anaphylactic reactions, 72–73, 73b
atopic reactions, *73,* 73–74
latex hypersensitivity, 74–75, 74b, 75b
localized reactions, 74
Type III hypersensitivity reactions, 75–76
Type IV hypersensitivity reactions, *76,* 76–77, *77*
Tzanck cells, 310, 319

U

Ulcers and ulcer-like lesions, 12, *13*
immune system disorders
aphthous ulcers, 341–344
Behçet syndrome, 344–345
Crohn disease, 351–352, *352*
erythema multiforme, 346–347, *347*
hypersensitivity reactions, 347–349
lupus erythematosus, 349–351, *351*
Reiter syndrome, 345–346, *346*
infectious agents
actinomycosis, 338–339, *339*
deep fungal infections, *339,* 340–341, 340b
gonorrhea, 337–338, *338*
necrotizing ulcerative gingivitis, 339–340
syphilis, 335–337, *336*
squamous cell carcinoma, 353–356
traumatic or inflammatory lesions
necrotizing sialometaplasia (*see* Necrotizing sialometaplasia)
traumatic ulcers (*see* Traumatic ulcers)
Unilocular radiopaque, 17
Unstable angina, 201
Upper respiratory diseases
common cold, 263–264
influenza, 264–265
Urticaria, 618, *618*

V

Vacuolated cells, 387
Varicella-zoster virus infection
primary, 312–314, *313*
secondary, 314–315, *315*
Varicosity, 375–377, *376*, 376b
Vascular disorders
abdominal aortic aneurysm, 203–205, *204,*
atherosclerosis, 195–198, *198*
coronary heart disease, 201–203, 202b, *203*
hypertension, 199, 199t, 200–201
Raynaud disease, 205, *205*
stroke, *206*, 206–208
thromboembolic venous disorders, 205–206, 206b
Vascular stasis, *47,* 48
Vasoconstriction, *47,* 48
Vasodilation, *47,* 48
Ventricular fibrillation, 201
Ventricular hypertrophy, 36, *36*

Ventricular septal defect (VSD), *209,* 209–210
Verrucous carcinomas, 88, *88, 441,* 441–442, *442*
Verrucous leukoplakia, 398
Vesicle, 12, *12*
Vesicular lesions
  autoimmune diseases
    pemphigoid (*see* Pemphigoid)
    pemphigus vulgaris (*see* Pemphigus vulgaris)
  congenital or genetic diseases (*see* Epidermolysis bullosa)
  infectious viral diseases
    coxsackievirus (*see* Coxsackievirus infections)
    herpes simplex virus (*see* Herpes simplex virus (HSV) infection)
    Paramyxoviridae virus infections (*see* Rubeola)
    rubella, 318
  traumatic lesions (*see* Mucocele)
Vesiculobullous disease, 393
Violaceous lesions, 368
Viral infection, 91
Viral sialadenitis (*see* Mumps)
Vitamin D-resistant rickets, 578, *578*
Vitiligo, 622, *622*
von Recklinghausen disease of the skin (*see* Neurofibromatosis, type 2B)

W

Waldeyer ring, 66, *66*
Warthin tumor, 465, *465*
Warts, 622
Well-defined margin, 17, *18*
Wellness concept, 3
White blood cells
  lymphoma (*see* Lymphoma)
  neutropenia, 238–239, *239*
White lesions, 13, *13*
  genetic or congenital disorders, 396, *396*
  immune system disorders
    lichen planus, *395,* 395–396
  infections
    acute pseudomembranous candidiasis, 392–393, *393*
    hairy leukoplakia, *394,* 394–395
    hyperplastic candidiasis, 393–394, *394*
    parulis, 395
  normal structure/tissue variation
    Fordyce granules (*see* Fordyce granules)
    leukoedema, 387, *387*
  premalignant/malignant disorders
    leukoplakia, 398–400
    oral submucous fibrosis, 400–401, *401*
  traumatic and inflammatory lesions
    cheek chewing, *389,* 389–390
    chemical and thermal burns, 391–392, *392*
    frictional keratosis, 388–389, *389*
    geographic tongue, 388, *388*
    hairy tongue, 391, *391*
    linea alba, 389, *389*
White sponge nevus (WSN), 396, *396*
Whooping cough, 266
Wickham striae, 395
Wound contracture, 59–60, *60*
Wound healing
  complications of, *59,* 59–60, *60*
  factors affecting, 57, 59

X

X chromosome inactivation, 125–127
Xanthelasma, 14, *14,* 198, *198,* 618, *618*
Xerophthalmia, 147, 457
Xerostomia, 32, 599
X-linked, dominant genetic disease, 559
X-linked recessive disorder, *136,* 137, 138b

Z

Zygote, 131